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PYOGENIC LIVER ABSCESSES DUE TO *KLEBSIELLA PNEUMONIAE* (FRIEDLAENDER'S BACILLUS)*

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FRIEDLAENDER'S BACILLUS has not often been recognized as an etiologic agent in liver abscesses. In 1892, Potier[1] reported the finding, at autopsy of a sixteen-year-old girl, of a liver abscess from which *Klebsiella pneumoniae* was recovered. Other cases have been reported by Chalier,[2] Courmont, Dujol and Devic,[3] Eliason,[4] Carnot, Dumont and Libert,[5] Le Sourd and Draillard,[6] Hegler and Nathan,[7] Baehr, Shwartzman and Greenspan,[8] Boettiger, Weinstein and Werne[9] and Rothenberg and Linder.[10] In none of the cases was there any mention of the serologic type of the organisms recovered. It is the purpose of this paper to report 7 cases with autopsy findings in which serologic studies were carried out in an effort to identify the type of *K. pneumoniae*.

MATERIAL

The material presented is selected from 5698 autopsies performed during the years 1934 to 1941 inclusive at the Mallory Institute of Pathology of the Boston City Hospital. During this time, 52 cases with liver abscesses of all types were found, a general incidence of 0.9 per cent. It is of some interest to compare these figures with those reported by Keefer[11] from this institute in 1934: 75 cases of liver abscesses in 10,309 autopsies, an incidence of 0.7 per cent, for the years 1896 to 1933 inclusive. Bacteriologic studies were carried out in 32 of the cases reported by Keefer. In no case was *K. pneumoniae* identified as the etiologic agent. In the present series, bacteriologic studies were carried out in 30 cases, and *K. pneumoniae* was identified in 7, or 23 per cent.

CASE REPORTS

CASE 1. C. B. T. (B.C.H. 791,965), a 64-year-old man, was admitted on July 11, 1935, complaining of intermittent fever, chills and cough.

Two months prior to admission, the patient noticed that his breath had a foul odor. He stated that he had lost 14 pounds. Two weeks before entry, he began to suffer from "nervous indigestion." This was followed a week later by the sudden appearance of attacks of severe chills, fever and sweating. These episodes lasted from 10 to 12 hours, after which he felt well until the next similar attack. Two days before admission, he developed a dry hacking cough. He also noticed thirst and polyuria. There was a history of diabetes of 3 years' duration.

On admission, the temperature was 101°F., the pulse 98, the respirations 24, and the blood pressure 120/80. The patient was well nourished and normally developed. The skin was warm and dry. The breath had a disagreeable and nauseating odor. The teeth were absent. The tongue was dry and coated. The prostate was large and boggy. There was a left indirect inguinal hernia. The remainder of the physical examination revealed nothing of note.

The hemoglobin was 76 per cent (Sahli), and the white-cell count was 13,600. A differential count showed 58 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 9 per cent monocytes and 1 per cent eosinophils. A strain of *K. pneumoniae* that did not ferment lactose was cultured from the urine. The urine showed various quantities of sugar but was otherwise normal. The blood Kahn and Hinton reactions were positive. Agglutination tests for typhoid, typhus and undulant fever were negative. Fasting blood-sugar determinations varied between 185 and 420 mg. per 100 cc.

The patient remained on the ward for 13 days, during which he experienced a severe chill on alternate days. On two occasions, a strain of *K. pneumoniae* that did not ferment lactose was cultured from the blood. Treatment was supportive. On the 13th day, the patient suddenly complained of marked shortness of breath. He became orthopneic and semicomatose, and died ½ hour after onset of these acute symptoms.

Autopsy (A-35-417). Nothing of note was found on external examination of the body. The liver, whose edge extended 8 cm. below the xiphoid in the midline and 3 cm. below the costal margin in the midclavicular line, weighed 2600 gm. The entire dome of the right lobe was fluctuant, and the capsular surface over this area was a mottled white and deep reddish blue. The capsular surface elsewhere was firm and a homogeneous reddish brown. On section of the right lobe, an abscess 12 cm. in diameter was found. The cavity of the abscess con-

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tained 150 cc. of thick, brownish-yellow glairy mucopurulent material, together with what appeared to be lumps of necrotic liver tissue. Sections taken from the wall of the liver abscess showed marked necrosis, with polymorphonuclear leukocytic and macrophagic infiltration. In sections taken from areas of the liver not adjacent to the abscess, large numbers of polymorphonuclear leukocytes were found in the sinusoids, together with small masses of bacilli, which were both intracellular and extracellular. There was a partially organized thrombus in one of the radicles of the hepatic arteries. Patchy groups of liver cells were vacuolated. The gall bladder and bile ducts were negative.

The spleen weighed 180 gm. The remainder of the gastrointestinal tract was not remarkable. There were also moderate atheromatous changes in the coronary arteries, an acute tracheobronchitis and aortic atherosclerosis.

K. pneumoniae and *Clostridium welchii* were grown from cultures of the liver abscess, pericardium, heart's blood, pleura and right upper lobe of the lung. The former did not ferment lactose.

Case 2. G. K. (B.C.H. 952,616), a 45-year-old man, first entered the hospital on July 2, 1938, complaining of a weight loss of 30 pounds in 5 weeks. In March, he had had an attack of diarrhea during which he had from ten to twelve stools daily. In May, he began to suffer from sharp pain localized in the right lower chest along the anterior costal margin; this was definitely worse on coughing and respiration. In June, he began to suffer from anorexia and fatigue. The family and past histories were irrelevant, except for excessive use of alcohol.

Physical examination showed only slight right-upper-quadrant tenderness. The red-cell count was 4,400,000 with a hemoglobin of 85 per cent (Sahli), and the white-cell count was 12,600, with 75 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes and 6 per cent monocytes. The blood Hinton reaction was negative. Nothing of note was found in the urine. On repeated tests of the stools 0 to +++ guaiac reactions were obtained; no parasites were found. Stool cultures were negative for pathogenic organisms. A blood culture showed no growth. Agglutination tests for the enteric group and *Brucella melitensis* were negative. A chest plate showed the right diaphragm to be slightly elevated.

The patient remained in the hospital 21 days. For the first 2 weeks he had a temperature that daily spiked to 101°F. but was afebrile during the 3rd week. Because he felt well, the patient left the hospital against advice.

The patient re-entered the hospital a month later, complaining of a recurrence of his original symptoms. He stated that his pain, which had shifted to the epigastric region, was gnawing, and that it was necessary for him to walk bent forward because of the pain. The temperature was 100.4°F., the pulse 104, the respirations 20, and the blood pressure 140/90. Physical examination was essentially the same as that at the time of his first admission.

The red-cell count was 3,310,000 with a hemoglobin of 61 per cent (Sahli), and the white-cell count was 18,800 with 78 per cent polymorphonuclear leukocytes, 4 per cent large lymphocytes, 17 per cent small lymphocytes and 2 per cent eosinophils. The white-cell count remained elevated during the remainder of the hospital stay. The alkaline blood phosphatase was 16.5 Bodansky units per 100 cc. The van den Bergh reaction was less than 1 mg. per 100 cc. The nonprotein nitrogen was 25 mg., the phosphorus 2.7 mg. and the calcium 9.2 mg. per 100 cc. Nine stools gave + to ++++ reactions to benzidine. No parasites were found in the stools. The bleeding time was 4½ minutes, and the clotting time 5 minutes. A sputum culture yielded a Type 13 pneumococcus and an alpha-hemolytic streptococcus. A blood culture was positive for *K. pneumoniae*, which was not acted on by Type A serum.

An x-ray film of the chest showed an area of cloudiness at the tip of the right diaphragm. The gastrointestinal series was interpreted as showing a duodenal ulcer with periduodenal adhesions.

The patient had a high, spiking temperature during his hospital stay and continued to complain of abdominal pain and to suffer from profuse sweats. In spite of supportive treatment, he died on the 31st hospital day.

Autopsy. (M. L. 30830.) The body was that of an emaciated man. The peritoneal surfaces were smooth and glistening. The liver weighed 2840 gm. and was adherent over the right lobe to the diaphragm. Attempts to separate these adhesions resulted in the opening of abscess cavities, which were filled with glairy, yellow, purulent matter. The abscesses in the liver were multiple, and varied in diameter from 0.5 to 6 cm. These were abundant throughout the left lobe and the upper portion of the right lobe, the external portion being fluctuant over considerable areas. Some of the abscesses, on the other hand, were relatively firm. Most of them were made up of single large cavities, but others showed a central cavity with yellow, opaque extensions about the border into the neighboring liver tissue.

Histologic sections showed massive destruction of liver tissue, with complete obliteration of the hepatic architecture. Around the periphery of the abscesses were large numbers of polymorphonuclear leukocytes and lymphocytes that infiltrated the remnants of the intact liver tissue. Bacilli, both intracellular and extracellular, were present in the abscesses.

The stomach was adherent over the internal surface of the left lower and spigelian lobes and lobus quadratus. It was impossible to separate the stomach wall from the liver. The mucosa of the stomach, even that portion above the esophageal junction, was greenish black. Patches of green necrotic material occupied the summits of the rugae of the upper fundus, where the wall was adherent to the posterior surface of the liver. In the lower fundus, the surface was irregular and firm, without evidence of stomach wall, and section disclosed necrotic underlying liver tissue, with no evidence of stomach wall. The duodenum was normal. Sections from the portion of the stomach adherent to the liver showed the wall to be completely necrotic, whereas those from uninvolved areas of the stomach revealed no lesion. The spleen weighed 400 gm. and was somewhat soft in consistence, but was not remarkable otherwise.

In addition, there were moderate atherosclerosis of the coronary arteries, bronchopneumonia of the left lower lobe and atelectasis of both lower lobes.

K. pneumoniae was grown from the heart's blood and from the liver abscesses. The capsule of this organism was not affected by Type A serum.

Case 3. C. F. (B.C.H. 931,709), a 71-year-old man, entered the hospital on February 27, 1939, too acutely ill to give an adequate history. The temperature was 101.4°F., the pulse was imperceptible, the respirations were 48, and the blood pressure was 80/60. The patient was in acute distress and markedly orthopneic, and the lips were

cyanotic. The skin was moist, cold and pale. The heart was enlarged to the left, and the sounds were muffled. Respirations were rapid and noisy, and there were fine, moist rales at the bases of both lungs. The abdomen was moderately distended, and the liver was enlarged to 5 fingerbreadths below the right costal margin. There was marked pitting edema of both legs. No laboratory work was performed.

The patient was given symptomatic and supportive treatment. He was digitalized rapidly. His condition became progressively worse, and he died the day after admission.

Autopsy (A-39-191). External examination of the body was negative. The liver weighed 1800 gm., was slightly increased in size and weight, was of a flabby consistence and was studded throughout by multiple, irregularly shaped abscess cavities containing very thick, mucoid, yellowish-brown exudate. The abscesses varied in diameter from 1 to 5 mm., and their walls were thin and shaggy. The wall of the gall bladder was markedly thickened, and the lumen contained three calculi varying from 1.0 to 1.4 cm. in diameter. The common duct could not be identified. Histologic sections of the liver showed marked post-mortem changes. There was a slight increase in the periportal connective tissue, together with moderate lymphocytic infiltration of these areas. There were multiple small abscesses in which the liver parenchyma was destroyed and replaced by polymorphonuclear leukocytes, bacilli and debris. The wall of the gall bladder was thickened by fibrous tissue and infiltrated by lymphocytes.

The spleen was markedly enlarged, weighing 1000 gm., and grossly showed no abnormalities. The splenic vein was normal. Microscopically, the pulp was diffusely infiltrated by polymorphonuclear leukocytes and markedly engorged by red blood cells.

The heart was moderately enlarged. There were pulmonary congestion and edema, and moderate benign prostatic hypertrophy.

Cultures from the hepatic abscesses revealed *K. pneumoniae* and an alpha-hemolytic streptococcus. Splenic culture revealed *K. pneumoniae*. The heart's blood was not cultured. The capsule of the Friedländer's bacillus did not react with Type A serum.

Case 4. W. P. (B.C.H. 955,438), a 65-year-old man, entered the hospital on September 21, 1939. He was drowsy and orthopneic, and was unable to give any history. From the patient's physician, it was learned that, 1 month before entry, the patient had complained of malaise. Examination of the urine at that time gave a positive test for sugar, which cleared following a restricted diet. Approximately 10 days before entry, the patient developed painless jaundice. On examination, the liver edge was palpated 2 fingerbreadths below the costal margin, and there was right-upper-quadrant tenderness. Two days before admission, the jaundice became severer, and the patient became semistuporous.

At the time of admission, the blood pressure was 100/50, the pulse 110, the respirations 35, and the temperature 101.8°F. The patient was obese, stuporous, dyspneic and breathing with Cheyne–Stokes rhythm. He appeared to be in extremis. The skin and mucous membranes were markedly icteric. Moist rales were present over the entire lower two thirds of each lung. The liver edge was palpated 1 handbreadth beneath the costal margin and was tender on pressure. The remainder of the examination revealed nothing of note.

The red-cell count was 3,500,000 with a hemoglobin of 65 per cent (Sahli), and the white-cell count was 18,300 with 87 per cent polymorphonuclear leukocytes, 7 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. The blood smear showed many young forms of the granulocytic series. The icteric index was 180. Tests for bile and urobilinogen were positive in 1:64 dilutions of the urine, which was otherwise normal. The blood Hinton reaction was normal. Lumbar puncture revealed nothing of note.

The patient was given supportive treatment but failed to respond and died a few hours after admission.

Autopsy (A-39-633). The body was that of a moderately well-nourished and well-developed man. There was marked icterus of the skin and scleras. Examination of the peritoneal cavity was negative. The liver weighed 2400 gm. Several irregular mottled yellow areas beneath the intact capsule contrasted with the reddish-brown parenchyma. On section, multiple abscesses, measuring a few millimeters to 8 cm. in diameter, were present. Microscopic sections of the liver showed marked replacement of the liver cells by scar tissue. There was polymorphonuclear leukocytic and lymphocytic infiltration about the smaller bile ducts, with moderate polymorphonuclear leukocytic infiltration of the ducts. Sections taken from the edges of the abscesses showed massive tissue destruction, together with masses of polymorphonuclear leukocytes. Groups of bacilli were present in the abscesses and were both intracellular and extracellular.

The mucosa of the common duct was dull red, and sections showed slight polymorphonuclear leukocytic infiltration. There was no evidence of stone or obstruction in any of the large bile ducts. The gall bladder was enlarged but was thin walled, and microscopic sections showed a slight degree of chronic cholecystitis.

The spleen weighed 300 gm., but was otherwise normal. The pancreas was grossly normal, but microscopic sections showed focal areas in which the intralobular and extralobular fat was necrotic and infiltrated by polymorphonuclear leukocytes. There was also moderate focal infiltration by polymorphonuclear leukocytes between the acini.

Bronchopneumonia and benign nephrosclerosis were present.

Cultures from the heart's blood showed *Escherichia coli*; from the bile, *K. pneumoniae*, *Cl. welchii* and *Esch. coli*; from the liver abscesses, *K. pneumoniae* and *Cl. welchii*; and from the right and left lower lobes, *K. pneumoniae*, pneumococcus (Type 29) and *Cl. welchii*. In each instance, the *K. pneumoniae* showed no reaction with Type A serum.

Case 5. E. G. (B.C.H. 958,180), a 41-year-old woman, entered the hospital with a chief complaint of right-upper-quadrant pain radiating to the right subcapsular region, and progressively increasing jaundice for the previous 3 days. The patient had been nauseated and had several bouts of vomiting before admission. No bile was seen in the vomitus. She had had no chills or sweating, but had had a fever. There had been no constipation or diarrhea. The stools were clay colored.

The patient had had many previous admissions to the hospital, several for rheumatic heart disease with mitral stenosis, auricular fibrillation and symptoms of decompensation, for which she was given digitalis. For the preceding 15 years, she had had symptoms relating to the biliary tract, for which she first had biliary drainage with removal of gallstones and later cholecystectomy and removal of calculi from the common duct. She had continued biliary symptoms with operations for removal of common-duct stones, and finally anastomosis of the com-

mon bile duct to the duodenum was performed 7 months before admission, because of a stricture of the common duct.

The blood pressure was 120/80, the temperature 103°F., the pulse 100 to 120, and the respirations 30. The patient was markedly jaundiced, thin and dehydrated. The diaphragm was not elevated, and a few basal rales bilaterally were heard in the lungs. The heart was moderately enlarged to the left and right, and the rate was rapid and grossly irregular. No murmurs were heard, and there were no thrills. There was no rigidity of the abdomen. There was tenderness in the right upper quadrant and epigastrium, but no masses were felt. The liver and spleen were not palpable. Peristaltic movements were present. Otherwise, physical examination was negative.

The urine showed a slight trace of albumin, rare white cells, and a ++++ test for bile, but was otherwise normal. The red-cell count was 3,580,000 to 3,260,000 with a hemoglobin of 70 per cent (Sahli), the white-cell count 18,000 to 29,800, and the icteric index 95. The fasting blood sugar was 96 mg. and the nonprotein nitrogen 47 mg. per 100 cc. The stools were clay colored. The blood Hinton reaction was negative.

The patient was placed on bed rest, with a high-carbohydrate intake. She was given one injection of vitamin K intramuscularly. She seemed to be improving but the jaundice did not decrease. On the 3rd hospital day she became very orthopneic and disoriented, and died on the following day.

Autopsy. (A-40-541.) The body was that of a well-nourished, markedly jaundiced woman. The peritoneal cavity contained no free fluid, and the surfaces were smooth and glistening. The liver weighed 2120 gm. and on section showed multiple abscesses scattered throughout, measuring from 0.4 to 1.5 cm. and filled with thick mucoid yellowish-green pus. Microscopically, sections showed marked necrosis of the parenchyma, with massive polymorphonuclear leukocytic infiltration and abscess formation. Many bacilli were present. The bile radicles were moderately dilated. The common duct was greatly dilated, measuring 3.0 cm. in circumference, and thickened, and had a functioning anastomosis to the duodenum. The gall bladder and cystic duct were absent. No calculi were found in the common duct. The spleen weighed 310 gm. and was normal.

There were healed rheumatic heart disease, with mitral stenosis, pulmonary congestion and edema, purulent leptomeningitis, and slight, healed pyelonephritis.

Cultures of the liver abscess showed *K. pneumoniae*. The capsule of this organism was not reacted on by either Type A or Type B serum. Cultures of the meninges yielded a Type 14 pneumococcus.

Case 6. P. S. (B.C.H. 1,005,913), a 56-year-old man, entered the hospital on May 4, 1941, complaining of a "cold" of 3 weeks' duration. He had been previously treated for diabetes mellitus in this hospital in November, 1940, and discharged on diet and insulin. He apparently did well until 3 weeks before entry, when he developed an upper respiratory infection. Two days before admission, he began to suffer from severe, persistent left-upper-quadrant pain, together with loss of appetite and dizziness.

The temperature was 99.2°F., the pulse 90, and the respirations 22. The blood pressure was 110/80. Physical examination showed a man who presented evidence of weight loss. There were moist rales at the base of the left lung. There was a systolic murmur at the base of the heart. A left indirect inguinal hernia was found. The remainder of the physical examination was negative.

The red-cell count was 4,400,000 with a hemoglobin of 88 per cent, and the white-cell count was 15,800 with 75 per cent polymorphonuclear leukocytes, 15 per cent small lymphocytes, 2 per cent large lymphocytes, 7 per cent monocytes and 1 per cent basophils. The blood nonprotein nitrogen was 25 mg., the calcium 9.2 mg., the phosphorus 2.8 mg., and the alkaline phosphatase 5.8 Bodansky units per 100 cc. The blood Hinton reaction was negative. The urine was acid, with a specific gravity of 1.014, a slight trace of albumin and a moderate amount of sugar. The urinary sediment was negative. The stool gave a ++ guaiac reaction.

The hospital course was one of progressive decline. The diabetes was easily controlled, but the patient continued to suffer from left-upper-quadrant pain and anorexia. He was given therapeutic doses of sulfathiazole. He gradually became weaker and incontinent, and died on the 27th day after admission.

Autopsy (A-41-423). The body was that of a normally developed but rather emaciated man. External examination revealed nothing of note. There was 150 cc. of fibrinopurulent exudate in the peritoneal cavity, and the peritoneal surfaces were covered by similar exudate. The lower surface of the liver, both kidneys and adrenal glands, spleen and pancreas all formed part of a large mass bound together by fibrinopurulent material. In the lesser peritoneal cavity and extending retroperitoneally was a large abscess containing foul brown pus. The duodenum formed one wall of this abscess, but the lumen was not affected. The celiac and superior mesenteric arteries contained large friable thrombi almost completely filling their lumens. The splenic vein was completely occluded by a friable necrotic clot, together with considerable purulent material. The portal vein showed thrombosis and purulent matter, which could be traced into the parenchyma of the liver.

The liver weighed 2030 gm. The capsule was intact. The surface and parenchyma were deep red, spotted by many irregular, pale yellow gray areas, which measured from 0.2 to 5.0 cm. in diameter. The centers of many of these areas were soft and necrotic and filled by creamy yellow mucopurulent material. It was estimated that these pale areas occupied two thirds of the liver substance. Microscopically, sections from the liver showed many abscesses, with necrotic liver cells, polymorphonuclear leukocytes and bacilli. The majority of the abscesses appeared to originate in the portal spaces. The walls of the abscesses showed marked polymorphonuclear leukocytic infiltration.

The portal vein was lined by an organizing, centrally liquefied thrombus. There was diffuse polymorphonuclear leukocytic infiltration of the vessel wall and surrounding tissue. A section taken from the splenic vein showed essentially the same process.

The wall of the gall bladder was markedly thickened by fibrous tissue and averaged 0.8 cm. in width. At the fundus was a large pocket of pus, which was walled off from the lumen. The lumen of the gall bladder contained pale, mucoid, slightly purulent bile. There was diffuse lymphocytic infiltration of the wall. Throughout the wall were focal masses of polymorphonuclear leukocytes. The walls of the cystic and common ducts were thickened and contained pale bile similar to that in the gall bladder.

The pancreas was soft and friable, and contained many irregular, rough stones averaging 0.2 to 0.6 cm. in di-

ameter. Most of these stones were surrounded by brown pus and were contained in small cystic spaces.

Sections from the pancreas showed a large portion of the parenchyma to be replaced by masses of polymorphonuclear leukocytes or diffusely infiltrated by lymphocytes and fatty macrophages. One section showed proliferation of atypical duct epithelium growing in a definitely circumscribed nodular arrangement. However, the tumor was growing along a nerve sheath in one area. This was interpreted as an early adenocarcinoma of the head of the pancreas.

In addition to the above lesions, there were a chronic gastric ulcer and healed focal pyelonephritis.

K. pneumoniae was cultured from the heart's blood, the liver abscesses, the gall bladder and the peritoneal abscess. It reacted with Type A serum.

Case 7. P. K. (B.C.H. 1,033,148), a 71-year-old man, was admitted in a semistuporous condition on July 19, 1941. Three weeks previously, he experienced a sudden onset of vague upper abdominal pain, which persisted for 1 day. The pain was accompanied by a temperature of 101°F. and was followed by slight jaundice, which disappeared after 2 days. The patient was treated with sulfanilamide and digitalis. The pulse and temperature became normal; the sulfanilamide was omitted, but the digitalis was continued. The patient remained drowsy, however, and the only complaint was that of difficulty in urinating. On the evening before entry, he had a shaking chill, and the temperature rose to 103°F. The past history was irrelevant.

At the time of admission, the temperature was 97.8°F., the pulse 80, and the respirations 20. The blood pressure was 110/54. Physical examination revealed a very acutely ill, well-nourished, stuporous man. The trachea was deviated to the left, and there was marked limitation of expansion of the entire left chest; over the same area, there were dullness to flatness, diminished breath sounds and diminished tactile fremitus. The heart sounds were distant, and the cardiac rhythm was regular. There was a short, rough, systolic apical murmur transmitted to the axilla and base. The abdomen was soft and rounded. A sharp, firm, nontender liver edge was felt 3 cm. below the right costal margin. There was no tenderness or spasm. The prostate was symmetrical, movable, moderately enlarged and nontender. The remainder of the physical examination was negative.

Examination of the urine revealed specific gravities varying between 1.006 and 1.020, a mild albuminuria and persistent moderate pyuria. Urine cultures constantly showed *K. pneumoniae*, *Esch. coli* and enterococci. Examination of the blood showed a red-cell count of 2,900,000 with a hemoglobin of 62 per cent (Sahli), and a white-cell count of 16,000 with 53 per cent polymorphonuclear leukocytes, 36 per cent band forms, 2 per cent metamyelocytes, 1 per cent myelocytes, 1 per cent basophils, 3 to 5 per cent lymphocytes and 3 to 5 per cent monocytes. The mean corpuscular volume was 107 cu. microns, the mean corpuscular hemoglobin concentration 31 per cent, and the mean corpuscular hemoglobin 33 microgm. The blood Hinton reaction was negative. The total serum protein was 5.6 gm. per 100 cc., with an albumin-globulin ratio of 1.0. The icteric index was 3. The formol-gel test was weakly positive. A bromsulfalein test showed 70 per cent retention of the dye in 5 minutes, and 20 per cent in 15 minutes. The prothrombin time was normal, and urobilinogen was present in the urine in a 1:2 dilution. Blood cultures yielded no growth. Gastric analysis showed 32 units of free acid before and 92 units after histamine; the fluid was guaiac negative. Guaiac tests of the stools were repeatedly negative.

X-ray study of the chest was negative. A gastrointestinal series was interpreted as showing an old duodenal ulcer, with perigastric adhesions and a hiatus hernia. A spot film of the gall bladder showed no evidence of gallstones. Two barium-enema studies were unsatisfactory.

The patient remained semistuporous throughout his hospital stay. During the 1st week, he had three shaking chills, the temperature spiking from 102 to 103°F. Sulfadiazine therapy was instituted, and blood concentrations reaching 10 mg. per 100 cc. were attained. During the 2nd week, the patient was afebrile, and sulfadiazine was omitted. During the ensuing 3 weeks, he had intermittent, low-grade fever. Accordingly, sulfadiazine was started again and continued for about 2 weeks, after which, because of continued fever, sulfathiazole was substituted and continued until the patient's death. The laboratory and physical findings remained essentially unchanged. During the final 2 days in the hospital, the patient began to vomit and became comatose. The nonprotein nitrogen rose to 83 mg. and the sulfathiazole level to 21 mg. per 100 cc., and the patient died quietly at the end of the 10th week in the hospital.

Autopsy (A-41-643). External examination of the body revealed nothing of note. The liver weighed 1600 gm. The capsule was smooth and glistening, and through it could be seen small, irregular areas, lighter in color. On section, numerous abscesses ranging from 2.5 to 5.0 cm. in diameter were seen throughout the right quadrate and caudate lobes. These abscesses were filled with a greenish-yellow, thick, tenacious exudate with a glairy appearance. The walls of the abscesses were irregular and contained fibrous connective tissue microscopically. The walls of the abscesses were diffusely infiltrated by polymorphonuclear leukocytes, and many bacilli were present. Patchy cholangitis of the small ducts and a slight degree of old biliary cirrhosis were noted. The gall bladder was small and almost entirely embedded in the liver substance. The walls were thickened to 4 mm. and, microscopically, were found to be studded with minute intramural abscesses. The lumen contained numerous facetted pigment calculi measuring up to 3 cm. in diameter, which were bathed in an exudate similar to that found in the liver abscesses. The common bile duct, which was slightly dilated, contained bile but no calculi. The portal vein showed no evidence of phlebitis.

There was no evidence of inflammation about the appendix or the numerous diverticulums of the sigmoid colon. The spleen weighed 60 gm. and was normal. The kidneys showed a slight amount of chronic pyelonephritis and retention of sulfathiazole crystals in the pelvis. The prostate contained active infection and at least one healing abscess. Unfortunately, no culture was taken. There were moderate edema and congestion of the lungs. The heart was negative. The vertebral bone was quite fatty and hypoplastic.

No organisms were cultured from the heart's blood. *K. pneumoniae* was cultured from the liver, the liver abscesses and the gall bladder; the strain reacted with Type B serum.

Discussion

A careful study was made of the clinical histories, signs and symptoms of our cases and of

those reported in the literature. No single sign or symptom was found that would distinguish liver abscess due to *K. pneumoniae* from those in which the usual pyogenic organisms were the etiologic agents.

The only laboratory finding of value in the diagnosis of liver abscess due to *K. pneumoniae* was the blood culture, which was positive in 11 of 23 cases reported in the literature. In the cases reported above, ante-mortem blood cultures were taken in 6, and *K. pneumoniae* was recovered in 1.

Pathology

The gross appearance of the liver abscess due to *K. pneumoniae* is, except for the exudate, similar to that in abscesses caused by other pyogenic organisms. In all but 1 of the cases presented above, there was multiple abscess formation. Of the 23 cases in the literature, the livers in 2 contained a single abscess. Two abscesses were found in one case, and three in another, whereas the livers of the remaining cases showed multiple abscess formation.

The exudate in all the cases presented above was characteristically glairy and mucoid. The exudate appears similar in all respects to that seen in *K. pneumoniae* infections of other parts of the body.

Microscopically, there is nothing to distinguish these abscesses from other pyogenic liver abscesses except for the finding of organisms with the morphology of *K. pneumoniae*.

Disease of the biliary system other than the liver was present in 4 of the 7 cases in the present series, in only one of which (Case 5) there was definite obstruction of the common bile duct; another (Case 6) was associated with acute suppurative cholecystitis and cholelithiasis, acute suppurative pancreatitis, early adenocarcinoma of the head of the pancreas and acute pylephlebitis. Case 7 was associated with acute empyema of the gall bladder, with cholelithiasis but no infection of any of the hepatic bile ducts. Case 3 was associated with chronic cholecystitis with cholelithiasis. In Case 2, the abscess resulted from direct extension from the stomach. It appears from this small series of cases that the pathogenesis of liver abscesses due to *K. pneumoniae* is varied and is similar to that of other pyogenic liver abscesses. In Cases 1 and 4, there was no associated biliary, gastrointestinal or urinary-tract infection.

Only 15 cases were found in the literature with reports complete enough to allow consideration of etiologic factors. Ten were associated with extrahepatic biliary disease. Of the remaining 5 cases, 1 was complicated by bronchopneumonia and empyema due to *K. pneumoniae*; 1 followed acute appendicitis, and 1 was associated with bronchiectasis and lung abscess from which Friedländer's bacillus was cultured. In the other 2 cases, no definite source of infection could be determined.

Bacteriology

Until recent years, *K. pneumoniae* has been associated in the minds of most observers as occurring primarily in the upper respiratory tract. This undoubtedly is largely because Friedländer,[12] in first describing the organism in 1882, named it the pneumobacillus and regarded it as the etiologic agent in lobar pneumonia. Even after Weichselbaum[13] demonstrated that the pneumococcus was the cause of lobar pneumonia, *K. pneumoniae* was always considered the agent responsible for a particularly malignant type of lobar pneumonia. Very little attention was given to the organism as an infective agent in other parts of the body, although numerous reports described the bacillus as causing suppurative lesions in practically every organ of the body. It has also been described as occurring in many domestic animals.

In 1937, Baehr, Shwartzman and Greenspan[9] reported a study of 198 cases of infection with Friedländer's bacillus. In this series, there were 25 cases of lung or upper-respiratory-tract infection, only 2 of which were cases of pneumonia in which the clinical and bacteriologic evidence indicated that *K. pneumoniae* was the primary cause of pneumonia. In 7 other cases of pneumonia, the authors recovered this organism in association with the pneumococcus or streptococcus. It is the experience of this laboratory that Friedländer's bacillus usually occurs as a secondary invader rather than as the primary organism in cases of lobar pneumonia and bronchopneumonia. In the series of Baehr, Shwartzman and Greenspan, the bacillus occurred in the gastrointestinal tract in 61 cases, in the genitourinary tract in 56, and in the biliary system and liver in 46.

It has been pointed out by Dudgeon[14] and Kendall[15] that the Friedländer bacillus is often found as a normal inhabitant of the intestinal tract.

The cultural and morphologic characteristics of the Friedländer bacillus are well known and need not be described here. However, comparatively little attention has been given to the type specificity of the various strains of this organism and to their clinical significance. Many unsuccessful attempts have been made by various investigators to arrive at a satisfactory classification of the Friedländer group by fermentation of the sugars. It was not until Julianelle,[16] in 1926, developed a serologic classification that any order was brought to this group. He found that there are three sharply defined and specific types and one heterogeneous

group of *K. pneumoniae*, and that the agglutination, agglutinin adsorption, protection, thread and precipitin reactions are highly specific for each type. Edwards,[17] who was able to confirm the work of Julianelle, demonstrated only two serologic types; a Type 1, which was mainly of equine origin and corresponded to Julianelle's Type B, and a Type 2, which was of human origin and corresponded to Julianelle's Type A.

Julianelle[18] carried out further work in which he studied eighty strains of *K. pneumoniae* gathered from various sources. He found 52 per cent to be Type A, 15 per cent Type B, 9 per cent of Type C and 24 per cent Group X. Type A, for the most part, consisted of strains derived from man, and more than 70 per cent of these were associated with pneumonia in human beings. The greatest number of Type B strains came from animal sources. The strains from heterogeneous Group X were found in a great variety of diseases.

Before the serologic typing of the organisms in the cases presented is discussed, it should be pointed out that Type A serum has been available here only since 1939, whereas Type B serum was first obtained by this laboratory in 1940. To date, Types C and X serums have not been obtainable.

Of the 7 cases presented above, the organism in only 1 case (Case 6) reacted with Type A serum. This is of particular significance, because this type, in the experience of this laboratory, is usually associated with respiratory infections. According to Perlman and Bullowa,[19] of 37 cases of Friedländer pneumonia, 29 were caused by Type A and only 8 were caused by Type B. Solomon[20, 21] reported similar results: in 9 cases of chronic Friedländer pneumonia, 7 were caused by the Type A strain, 1 by the Type B and 1 by the Type C; and in 10 cases of acute Friedländer's pneumonia all were caused by the Type A strain.

The organism in Case 7 belonged to Type B. Again, there were no lung lesions and the blood culture was negative.

The bacilli from Cases 2, 3 and 4 were not reacted on by the Type A serum, and therefore belong to Type B or C or Group X, whereas the capsules of the organisms in Case 5 did not swell in the presence of either Type A or B serum. The patient in Case 1 was autopsied before any serum was available, and thus the organism was not serologically typed. However, it was not a lactose-fermenting organism, and it has been the experience in this laboratory that the Type A organisms are lactose fermenters.

Recently, a case of common-duct obstruction with pericholangitis and empyema of the gall bladder came to autopsy. Friedländer's bacillus was cultured from the liver and the gall bladder. This organism was not reacted on by either the Type A or the Type B serum.

To summarize, 1 case of biliary tract infection was infected with the Type A organism, whereas 6 were definitely not. To this group, the case that was not typed could in all probability be added. Of these 7 cases, 3 are known definitely not to belong to Type B. Although the number of cases presented is too small to draw definite conclusions, it is interesting to draw attention to the large preponderance of organisms other than those classified as Type A in these hepatic infections.

Summary

Seven cases of liver abscess due to *Klebsiella pneumoniae* (Friedländer's bacillus) are reported, and the autopsy and bacteriologic findings are discussed. One case of empyema of the gall bladder and cholangitis due to Friedländer's bacillus is mentioned.

The significance of the serologic typing of Friedländer's bacillus is discussed. In the cases presented, all but one of the organisms belonged to serologic groups other than Type A.

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THE FAILURE OF COBRA VENOM TO RELIEVE PAIN IN RHEUMATOID ARTHRITIS*

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BOSTON

PAIN is the greatest single factor responsible for restricted joint motion, subsequent muscle atrophy and articular deformity in rheumatoid arthritis. The course and outcome of this disease would presumably be more favorable if pain could be completely controlled. Unfortunately there is no analgesic capable of producing such an ideal situation, although the salicylates, especially acetylsalicylic acid (aspirin), administered in maximal dosage most nearly approach this goal.

The use of cobra venom was suggested by reports of its analgesic action not only in cancer[1-3] but also in various rheumatic diseases.[2, 4] Macht[1] attributes its effect in human beings to a central action on the higher cerebral nerve centers. In comparison with morphine it is supposed to produce a more delayed but longer-lasting analgesia.

Moderate success has already been claimed for its use in arthritis. Although Macht[2] thought that the 10 arthritis patients treated by him formed too small a group to warrant discussion, he noted that "considerable relief of pain has been obtained in some instances." Steinbrocker and his associates[4] reported that 11 of 13 patients with rheumatoid arthritis experienced slight to moderate improvement. Varying degrees of benefit were observed in other patients with degenerative joint disease, so-called "fibrositis" and "neuralgia." The reports of Burkhardt,[5] who used intracutaneous injections of venoms from *Vipera aspis* and *Vipera ammodytes*, and that of Butler,[6] who administered copperhead venom intradermally, are not sufficiently detailed to allow evaluation of their results. Because of the need of a more ideal analgesic in rheumatoid arthritis it has seemed advisable to attempt to corroborate these reports.

METHOD OF STUDY

Availability and the presence of pain were the criteria for the selection of 12 patients with unquestionable clinical, laboratory and x-ray evidence of rheumatoid arthritis. Each patient served as his own control, having been observed for several months to several years before treatment. All were followed subsequently for four weeks to six months. Nine were hospitalized and on bed rest during the period of therapy; three were ambulatory, having been hospitalized previously. Physiotherapy and necessary orthopedic measures were continued, but acetylsalicylic acid was omitted in all but 1 case. All patients were seen daily by the same observer and evidence of objective as well as subjective improvement was noted. Measurements of pain thresholds were made in 4 patients. Laboratory data relative to blood cytology, urinalyses and corrected sedimentation rates[7] were obtained in all cases.

Cobra venom§ was administered intramuscularly each day. Larger doses were employed than had been used by Macht[1] (5 mouse units daily until relief of pain was noted) and Steinbrocker et al.[4] (10 mouse units daily to a total dosage of 50 units before considering the result a failure). Our first 2 patients received 10 units daily for four to six days, then 20 units a day for three to four days, and eventually 30 units every twenty-four hours. All other patients were given 10, 20 and 30 mouse units on each of the succeeding first three days and 30 units daily thereafter. A total of at least 300 mouse units was given in all cases, a dosage adequate to demonstrate any analgesic action of cobra venom.

RESULTS

The data of the individual cases are shown in Table 1.

Toxicity

No serious toxic effects were noted with the large doses employed. In Case 2, the patient experienced a transitory sedative effect on several occasions. Local reaction at the site of injection occurred in only 1 patient (Case 12). In this case, ninety minutes after each injection there appeared an irregular erythematous area, 2 cm. in diameter, which was accompanied by local heat. There was marked local pain for five to twelve hours. After twenty-four hours a 1-cm. ecchymotic, slightly elevated, warm induration persisted, which slowly disappeared in the course of several days.

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From the Medical Clinic, Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.

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§Dr. David I. Macht of Hynson, Westcott and Dunning, Incorporated, Baltimore, kindly supplied the cobra venom used in this study. The preparation contained 10 mouse units per cubic centimeter of solution.

Table 1. *Summary of Clinical Data.*

Case No.	Patient	Sex	Age	Duration of Disease	Severity of Disease	Previous Treatment and Effect	Stage of Disease	X-ray Findings	Sedimentation Rate		Total Dosage of Cobra Venom	Analgesic Effect of Acetylsalicylic Acid	Remarks
									before therapy	after therapy			
				yr.					mm./min.	mm./min.	mouse units		
1	G. L. (No. 168146)	M	26	4	Marked; progressive.	Hospitalization, orthopedic measures, theelin and Relaxin, with temporary benefit	Exacerbation; increased pain.	Osteoporosis of spine; fusion of sacroiliac joints; narrowing of hips.	0.46	0.52	345	Good	Hip pain increased while taking cobra venom; no objective changes; acetylsalicylic acid far superior.
2	S. K. (No. 60132)	M	22	8	Marked; progressive (2 yr.); in bed (1 yr.).	Hospitalization and orthopedic measures, with slight benefit	Active; constant pain in all joints.	Narrowing of joint spaces, with bony fusion in some	1.54	1.67	355	Poor	Less pain and stiffness noted after 175 units; no objective changes; patient evaluated 50–75 per cent relief of pain; occasionally felt sleepy after an injection.
3	A. B. (No. 157841)	M	55	5	Marked; progressive.	Hospitalization, vaccines, transfusions, vitamin D, bee venom and gold (2 courses) with no benefit	Active; constant pain in all joints.	Irregular narrowing and destruction of wrists, hands and elbows	1.92	Not done	395	Poor	No subjective or objective change
4	M. V. (No. 226089)	F	29	18	Moderate; prior remission with pregnancy, lasting 8 yr.	None	Active; exacerbation for 8 mo.; moderate pain.	Destructive changes of joint margins of some interphalangeal joints	0.74	0.72	440	Good	Claimed 25–50 per cent relief of pain, starting after 175 units; no objective changes; as good results with acetylsalicylic acid.
5	H. H. (No. 127252)	F	49	10	Moderate; remission in past for 5 yr.	None	Active; exacerbation for 6 mo.; severe pain.	Decalcification; narrowed finger joints and hips, with some destruction	1.28	1.58	300	Fairly good	No relief of pain; acetylsalicylic acid superior.
6	E. A. (No. 327707)	F	40	3½	Moderate	None	Moderately active	Destruction of some interphalangeal and carpal joints	0.91	0.86	300	Good	No relief of pain; acetylsalicylic acid superior.
7	A. B. (No. 321644)	F	53	2½	Marked; progressive.	Serum injections, with no benefit	Active; severe pain in all joints.	Widespread decalcification; narrowing of many joints	1.25	1.1	300	Good	Increased pain while taking cobra venom; acetylsalicylic acid far superior.
8	E. A. (No. 159185) ambulatory	M	40	5½	Moderate	Hospitalization and arthrodesis of ankle, with slight benefit	Mildly active; moderate pain.	Narrowing of left wrist and sacroiliac joints	0.33	Not done	300	Fair	Increase in pain to point of incapacitation while taking cobra venom; acetylsalicylic acid far superior.
9	H. N. (No. 184822) ambulatory	F	29	10	Mild; several remissions.	Hospitalization, physiotherapy and orthopedic measures, with moderate benefit	Mildly active; no objective changes.	New bone formation about sacroiliac joints	0.36	0.17	300	Poor	Less constant back pain after 180 units; return of constant pain within 36 hr. after medication stopped; better than acetylsalicylic acid.
10	C. K. (No. 69971) ambulatory	M	54	8	Moderate; remission in past.	Hospitalization, with moderate benefit	Acute exacerbation; increased pain and marked constitutional symptoms.	Decalcification of tarsal and carpal bones	1.57	1.68	300	Good	No benefit from cobra venom; unable to do without acetylsalicylic acid at any time.
11	G. M. (No. 173005)	F	62	7	Moderate; progressive.	Synovectomy, both knees, and gold, with moderate benefit	Active; exacerbation with severe pain and iritis.	Decalcification; narrowing and irregularities of joints of hands and feet.	1.58	1.42	300	Good	Increased pain during treatment, and joint motions more restricted
12	C. O'B. (No. 345635)	F	37	10	Moderate; slowly progressive; remission in past with pregnancy.	None	Active; exacerbation for 1 yr., moderate pain.	Narrowing of joint spaces; some joint destruction in hands, wrists and feet.	0.61	0.38	300	Good	Increased pain while taking cobra venom; local reactions at site of injection; frequently requested acetylsalicylic acid for relief.

Subjective Improvement

Three of the 12 patients (Cases 2, 4 and 9) experienced some degree of subjective improvement. In Case 2 the patient claimed 50 to 75 per cent relief, manifested by decrease in pain and stiffness, first noted after the administration of a total of 175 units. He considered the effect superior to that of acetylsalicylic acid. In Case 4 the patient admitted 25 to 50 per cent relief of pain, apparent after a total dose of 175 units, but stated that aspirin was equally effective. Both these patients were treated during exacerbations of the disease and had almost constant pain and stiffness. In Case 9, an ambulatory patient in a partial remission experienced about 50 per cent relief based on inconstancy rather than decreased intensity of pain after receiving 180 units. Acetylsalicylic acid was regarded by her as inferior. The prolonged analgesic effect attributed to cobra venom was not observed, since her symptoms increased within thirty-six hours after the drug was discontinued.

All nine of the remaining patients experienced either no relief or an actual increase in the amount of pain and stiffness, possibly owing to the withdrawal of acetylsalicylic acid. They invariably believed the latter to be a superior analgesic.

Objective Improvement

Reduction of articular swelling or effusion or increase in muscle strength or range of joint motion was not observed in a single individual. An attempt was made in Cases 1, 2, 3 and 4 to measure objectively the effect of cobra venom on pain threshold in order to note any correlation with subjective improvement. A modification[8] of the method of Hardy, Wolff and Goodell[9] was used, consisting essentially of determining the threshold for the pain produced by thermal radiation of the skin.* The relation between pain elicited in the skin by thermal radiation and that arising from a diseased joint is not established. However, the measurement employed offers the most satisfactory method available for obtaining objective evidence of reduced sensitivity to pain.

In Case 1, nine determinations were made before and during treatment. All results remained within the normal range expected for race and age. This agreed with the clinical response. One patient (Case 2), who derived the greatest benefit subjectively, showed an extremely high threshold of pain at first, but no change in eight subsequent tests during treatment. The lack of subjective relief in Case 3 coincided with the lack of alteration of pain threshold even after a total dose of 375 units. Subjective improvement in Case 4 was first admitted after 175 units. However, it was not until a total of 440 units had been given that it became possible to discern an appreciable elevation in pain threshold as objective evidence of relative hypoactivity.

Although the results of this study indicated a slight correlation between subjective and objective findings, the number of patients was too small to permit definite conclusions.

Laboratory Studies

No striking effect on the sedimentation rate was noted. In one patient (Case 2) who showed subjective improvement the rate rose from 1.54 to 1.67 mm. per minute, whereas another (Case 12), who had increased symptoms during treatment, showed a fall in the sedimentation rate from 0.61 to 0.38 mm. There were no appreciable changes in erythrocyte and leukocyte counts or hemoglobin content. Urinalyses did not deviate from normal. Neither febrile nor antipyretic effects were observed as a result of the venom.

Summary

The effects observed with large doses of cobra venom for the control of pain in rheumatoid arthritis were disappointing and contrary to previous reports. Three of 12 patients experienced subjective relief, estimated variably from 25 to 75 per cent. In no case was improvement complete, dramatic or lasting. There were no objective alterations. The only significant toxic effect was local reaction at the site of injection in 1 patient. Acetylsalicylic acid was considered to be as good or better as an analgesic by 10 of the 12 patients studied.

The results indicate that cobra venom is of no value for the relief of pain associated with rheumatoid arthritis.

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METHYL SALICYLATE POISONING

A Report of Five Cases

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THE danger of poisoning by oil of wintergreen has not been sufficiently emphasized. It is commonly used in the home, and may be accidentally ingested by children, who, as Shipley[1] points out, may associate the pleasant aroma with wintergreen-flavored candy. It is therefore wise to continue the reporting of such cases. I present a brief summary of the cases reported to date, and 5 additional cases, 2 of which were seen by me.

Lawson and Kaiser[2] in 1937 tabulated 43 cases from the literature and added 1 of their own. In the same year Stevenson[3] gathered 45 reported cases, 10 of which were not included in Lawson and Kaiser's summary, and added 3 of his own — making a total of 57. Not included by either author were 4 cases reported by Shipley[1] in 1933, and 1 case reported by Bowen, Roufa and Clinger[4] in 1936. In 1938, Kane[5] reported 2 cases, Eimas[6] 1 case, and Baxter, Hartwell and Reck[7] 2 cases. Donatelli and Abbate[8] reported 1 case in 1939, Shirreff and Pearlman[9] 2 cases in 1940, and Epstein and Work[10] 1 case in 1942. To this final total of 71 reported cases are added the 5 additional cases described below.

Thirty-seven of these 76 patients died. Twenty-three of the fatal cases occurred in children under five years of age. The smallest fatal doses were estimated at 4 cc. for a child one and a half years of age,[2] and 4 cc. for a two-year-old child.[3] A number of small children died from slightly larger doses. One death in a two-and-a-half-year-old child following the external administration of methyl salicylate was reported by Lawson and Kaiser.[2] The smallest fatal dose reported in an adult was 6 cc.[2] The largest estimated doses followed by recovery were 30 cc. for a child two years of age, and 30 cc. for several adults.[2, 8] However, dosage reports, even as estimates, are obviously only partially reliable, particularly in small children.

The usual more severe course involves vomiting, hyperpnea, diaphoresis, extreme thirst, dehydration, stupor and convulsions. In the fatal cases death commonly occurs within twenty-four hours. Kane[5] reported a patient who died two and a quarter hours after ingestion of the poison. The commoner pathological findings observed at autopsy in cases of methyl salicylate poisoning[11, 12] include acute degenerative nephritis, edema and fatty degeneration of the liver, congestion and edema of the lungs, acute gastritis and hyperplasia of the lymphoid structures in the intestinal tract, and small hemorrhages in the pericardial membrane and the pleurae and subdurally. Dodd, Minot and Arena[13] have studied the altered physiology in salicylate poisoning in general, and have discussed treatment rationale, including the necessity for administering large amounts of fluid and combating acidosis.

The 5 additional cases are as follows:

CASE REPORTS

CASE 1. A 2-year-old boy was brought to the office about 4 hours after having swallowed an estimated 15 cc. of methyl salicylate; this was followed by vomiting and alternate periods of restlessness and mild stupor. The chief features on his arrival were marked perspiration, rapid breathing and pale mucous membranes. Vomiting was mechanically induced. Following this procedure, a Levin tube was introduced and the stomach was thoroughly irrigated with a dilute solution of sodium bicarbonate. A definite oil of wintergreen odor was obtained from the aspirated fluid. The lavage was continued for a long period of time, until finally no odor of the drug could be detected. The patient was then sent to the hospital with a guarded prognosis.

Treatment at the hospital consisted chiefly in forcing fluids by mouth, including dilute solutions of sodium bicarbonate. Significant laboratory findings were acetone, diacetic acid and a trace of albumin in the urine and a white-cell count of 20,000. The child's symptoms and the urinary findings subsided fairly promptly. He was discharged home in good condition on the 3rd day.

CASE 2. A 55-year-old man was seen about 6 hours after having ingested one tablespoonful (15 cc.) of methyl salicylate for "heartburn." He was unaware of the toxicity of the drug for internal use. One hour after ingestion, the patient developed tinnitus, "a full head" and numbness of the upper and lower extremities. Two hours later he became hot, perspired freely and breathed rapidly. Because of intractable gagging with attempted use of the nasal tube, an automatic lavage was employed by having the patient drink huge quantities of a dilute solution of sodium bicarbonate, with consequent induction of vomiting. A strong oil of wintergreen odor was present in the vomitus. The treatment was continued for an extended period of time, until finally no odor could be detected. After vomiting, the patient stated that he felt better immediately and that the numbness had greatly decreased. The patient had no sequelae except for a transitory albuminuria.

Two urine specimens produced slight reduction of Benedict's solution, but the patient failed to co-operate with requests for further checking. It therefore is not

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known whether the copper reduction was the result of the salicylate or of a mild underlying glycosuria.

CASE 3.* A 2-year-old girl was seen in her home about 6 hours after she had ingested methyl salicylate. An estimated ounce (30 cc.) was missing from a bottle containing synthetic oil of wintergreen, but some had been spilled. An oil-of-wintergreen odor was present on the child's breath. There were rapid breathing and restlessness. The child was hospitalized.

In the hospital, hyperpnea was marked, the pulse was rapid, and pallor was present. The patient's condition appeared to become serious, and she was alternately listless and restless. Treatment consisted chiefly in stomach lavage, sodium bicarbonate medication and repeated saline hypodermoclyses. The patient showed improvement after 15 hours of treatment, and was well enough to be discharged home on the 3rd day.

CASE 4.† A child about 3 years old was seen in the accident room of the Cambridge City Hospital about ½ hour after the ingestion of oil of wintergreen. About one quarter of an ounce (7.5 cc.) was missing from the bottle, but some had been spilled. The patient vomited profusely, and further vomiting was then induced. As the patient did not appear ill, he was sent home without further treatment. About ½ hour later convulsions occurred, to which, however, the patient was said to be subject. Arrangements were made for immediate return to the hospital, but on arrival the patient was dead. Death had occurred within 2 hours after the taking of the poison.

CASE 5.† A 48-year-old woman was admitted to the Cambridge City Hospital 2 hours after having taken one teaspoonful (4 cc.) of methyl salicylate by mistake. She had vomited shortly afterward, noted ringing of the ears and felt nauseated. On entry, the patient's stomach was lavaged, and later 2000 cc. of 5 per cent glucose solution was given by clysis. No further toxic symptoms developed. The urinary findings were negative except for an "orange" copper reduction, which could have been due to the glucose medication. The patient was discharged home recovered on the 7th day.

DISCUSSION

The toxicity of oil of wintergreen should be more widely appreciated. Its poisonous nature when ingested should be stressed in medical schools, and among physicians and the laity. Bottles containing methyl salicylate should bear poison labels and be kept safely out of reach of children.

Cases 1, 2 and 5 suggest the value of prompt and thorough lavage. This procedure may very well have been the chief reason for the mild courses that followed. Lavage and the copious administration of parenteral fluids in Case 3 presumably aided in the recovery of this more seriously afflicted patient.

Treatment to rid the stomach of the poison must be adequate. Mere vomiting may induce a false sense of security. Indeed, more than one child has died after a parent has been told that its vomiting precluded the necessity for further treatment. Ordinary vomiting does not completely remove methyl salicylate from the stomach. Gastric lavage should be done when the patient is first seen, and should be prolonged until *no* trace of the drug odor is present in the washings. If the tube is not tolerated, an automatic lavage should be employed: that is the patient should be forced to drink huge quantities of water or of a dilute solution of sodium bicarbonate, with consequent induction of vomiting. To be adequate the process must be repeated again and again.

SUMMARY

The toxicity of methyl salicylate is emphasized, and proper treatment following its ingestion is discussed.

Five such cases of poisoning are reported.

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MEDICAL PROGRESS

HEMATOLOGY*

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BOSTON

DURING 1942, relatively little that is new or startling in the hematological field has occurred. Further developments with reference to the Rh factor and its relation to erythroblastosis foetalis have taken place; much has been written of transfusions, plasma and transfusion reactions; the hemolytic syndromes continue to occupy a prominent place; and the hemorrhagic states have received much attention. Leukemia remains as much of a problem as heretofore despite an initial flurry of enthusiasm for radio-phosphorus.

BLOOD CELLS

The matter of *elliptic erythrocytes* and *elliptocytosis* has been studied by Wyandt, Bancroft and Winship.[1] Eighty-six new cases in three large families of German extraction are reported. In all except 1 case, in which there was an associated spherocytosis, no anemia or other abnormality was present, and the condition was apparently without significance. All vertebrate animals with the exception of mammals have elliptic and nucleated red cells. The further exception to the latter statement is the camel, which has elliptic, non-nucleated red cells. It is probable that elliptocytosis is commoner than is generally recognized. This abnormality should not be confused with the elliptocytosis occurring in connection with the target cell and increased hypotonic resistance, noted chiefly in persons of Italian and Greek origin. There is a large group of syndromes affecting Mediterranean peoples, chiefly Italians, which is characterized in part by the presence of abnormally thin, hypotonically resistant target cells (so-called "leptocytes") and elliptocytes.[2] These disorders are inherited as a Mendelian dominant and vary in severity from the fatal Cooley's anemia to very mild conditions of no significance to the individual himself, but important from the hereditary standpoint.

The *target cell*, as noted in previous reviews, is assuming greater importance as it is realized that from the standpoint of thickness, three types of red cells can be discriminated: the normocyte, approximately 2.0 microns thick; the spherocyte, 2.5 to 3.5 microns thick; and the leptocyte, approximately 1.5 to 1.7 microns thick. The thicker the red cell, the more fragile it is to hypotonic salt solutions. The leptocyte is thus the antithesis of the spherocyte. Of interest is the fact that the former cell is present in large numbers in sickle-cell anemia. It is possible that the target cell, the oval cell and the sickle cell — when they are inherited — are more or less related. The target cell may occur, as Bohrod[3] has pointed out, shortly after hemorrhage; there it probably represents a relatively thin and somewhat younger red cell. To assume, as Bohrod does from the findings after hemorrhage, that the target cell is always simply a hyper-resistant young cell that appears in the blood following active bone-marrow regeneration seems illogical, since it is commonly found in persons without evidence either of blood loss or of increased blood destruction. In another paper, Bohrod[4] points to an increasing resistance of the bowl-shaped target cell to dilute acetic acid.

Schleicher[5] discusses at length the origin and nature of the *Cabot ring bodies* in erythrocytes. Although most authorities have considered them to be of nuclear origin, Schleicher presents evidence that they are actually the expression of a denatured or colloid protein connected with the nucleus and produced by the activity of a lysin on the lipoprotein constituents of the red cell.

The exact nature of the *eosinophil* remains obscure. It is certainly a granulocyte and thus a bone-marrow cell. However, its behavior with respect to pathologic processes differs strikingly from that of the neutrophilic granulocyte. Thus in acute pyogenic infections, with a sharp increase in polymorphonuclear neutrophils, the eosinophils drop out of the picture, whereas with subsidence of the infection they increase in number. Thus the eosinophil seems to have a reciprocal relation to the neutrophil. Why it becomes increased in allergic conditions and in such widely separated entities as parasitic infestation and periarteritis nodosa is not known. The stimulus that provokes the production and delivery of eosinophils to various parts of the body, and thus eosinophilia, is as yet obscure. An unusual, although by now well-documented, type of eosinophilia is that described by Loeffler of Switzerland in 1936, and often known as Loef-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

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fler's syndrome. This is characterized by a transient and rapidly shifting infiltration of the lungs, and is accompanied by relatively few symptoms, indicating a mild infectious process. Eosinophilia of 15 to 35 per cent, occasionally higher, is present. Neither the nature of the infection nor the cause of the eosinophilia has been determined. Elsom and Ingelfinger[6] report a probably related, if not identical, entity in 2 cases of eosinophilia and pneumonitis in chronic brucellosis. Both cases showed well-defined eosinophilia up to 42 per cent, peculiar pulmonary lesions and rather definite evidence of brucellosis. The cases known as Loeffler's syndrome were not studied for the question of undulant fever, and it is possible that both Elsom and Ingelfinger's cases and those of Loeffler and others may be peculiar examples of brucellosis with involvement of the lungs and with eosinophilia.

Infectious mononucleosis continues to present interesting diagnostic possibilities. It is a common infectious disease, and despite continued publicity is still frequently mistaken for other conditions. Mild fever in a young adult, particularly if he is a student or in some branch of the medical profession, should make one at least suspect the possibility of the disease. Severe headache ushers in most cases and may be mistaken for encephalitis, encephalomyelitis or kindred affections. The spinal fluid in these cases may show lymphocytosis and thus lead to the diagnosis of choriomeningitis or aseptic lymphocytic meningitis. Although the spinal-fluid lymphocytosis is generally regarded as a complication of the disease, it is simply indicative of the widespread lymphoid reaction which may result in perivascular collections of lymphocytes in the brain, and in serous meningitis. Zohman and Silverman[7] report a case with diffuse lower motor-neurone disease. The throat lesions, although mild in most cases, may be unusually severe in others and accompanied by marked swelling of the neck. If this is so, there is usually a complicating Vincent's infection for which a small dose of neoarsphenamine may be given intravenously. Rarely, the throat reaction may be due to a complicating pneumococcal infection that will respond readily to one of the sulfonamide drugs.

The blood picture shows a well-marked lymphocytosis with the presence of all varieties of lymphocytes, frequently bizarre in shape, size and staining characteristics. The absence of well-defined anemia and of reduction in platelets are two important criteria that should immediately rule out the diagnosis of acute leukemia. However, every rule has its exception. Thus, every so often one sees a case of thrombocytopenic purpura with well-defined lymphocytosis. The diagnosis of acute lymphatic leukemia is naturally made, although this can generally be ruled out when the great variability in lymphocytes is noted. In acute leukemia a monotonous blood picture is present, most of the cells being lymphoblasts. As Minot pointed out several years ago, many cases of idiopathic thrombocytopenic purpura present lymphocytosis in which some relatively young forms are rather common. That infectious mononucleosis will occasionally, particularly when splenomegaly is present, result in thrombocytopenic purpura is not well known. I have seen 2 such cases and Brooks[8] reports another.

A pink macular rash which fades readily on pressure is found occasionally. The mesenteric adenitis with its resultant abdominal pain may result in the diagnosis of acute appendicitis, especially since the leukocyte count is usually elevated. Straus[9] reports a case in which, although the white-cell count was low, — as it is in about 10 per cent of cases of infectious mononucleosis, — the diagnosis of acute appendicitis was made and operation performed. The appendix was the site of an atypical hyperplasia of the lymphoid tissue, which appeared identical with lesions previously described by Gall in enlarged lymph nodes. It is thus a good rule to consider the diagnosis of infectious mononucleosis in every febrile condition in a youngster or a young adult. Cases in very young children and in people above the age of thirty are unusual. The heterophil agglutination test, using sheep's red cells, is an important diagnostic criterion of the disease. It is positive in about 75 per cent of the cases. Why an antibody is produced that has the specific property of agglutinating sheep's red cells has not been determined, nor has any real advance been made in discovering the infectious agent. A virus etiology has naturally been suggested, and experiments indicating this as a possibility have been recorded by Wising[10] and by van den Berghe and Liessens.[11] These investigators introduced glands or blood from patients with the disease into monkeys and produced an infection with suggestive clinical and hematologic features.

Therapeutically, no real progress has been made. As noted above, a complicating Vincent's infection of throat or gums may indicate the use of neoarsphenamine, and sulfathiazole may be used with a complicating coccal organism. I have failed to find any value, however, in the routine use of the sulfonamide drugs, although Hoffman, Lees and Comroe[12] state that sulfathiazole appears to be of definite value in shortening the symptomatic stage of the disease. Lassen and Thomsen[13] claim benefit from the use of specific convalescent serum in doses of 60 to 300 cc. intravenously. This method probably deserves greater attention in this country

than it has heretofore received, although it must be conceded that most cases are very mild and require only symptomatic treatment. The best thing about the condition is, however, its 100 per cent recovery rate.

In the last few years, a new infection resulting in such phenomena as generalized lymphadenopathy and splenomegaly and caused by the *Histoplasmoma capsulatum* (Darling) has been described. Wright and Hachtel[14] illustrate a case report of histoplasmosis with some excellent photographs of the organism both in cultures and in tissues. The histoplasmoma is a fungus that has two forms. One is yeastlike and occurs in the blood and reticuloendothelial cells, whereas the other, a mycelial form, develops outside the body in cultures held at room temperature. The yeastlike forms grow only on blood or serum agar at 37°C.

Only about 35 cases have thus far been reported. The symptoms are variable, with irregular fever, lymphadenopathy and splenomegaly outstanding. There may be a moderate normocytic anemia, and leukopenia is usual. As Reid, Scherer, Herbut and Irving[15] point out in a case report, the parasites may be present within the blood cells and recognizable by ordinary blood smears. Sternal puncture in their case showed numerous monocytes and neutrophils containing inclusions resembling superficially Leishman-Donovan bodies. Blood culture is frequently positive, the organism growing out readily after several days either at room or incubator temperature. The disease is very serious and is often but not necessarily fatal. Therapy has not been successful, although antimony has been thought to be of some value.

Miscellaneous

An experimental study which may be of some clinical significance is that of Nettleship,[16] in which heterologous *bone-marrow antibodies* were produced and injected into the donor animal. An extract of rabbit bone marrow was repeatedly injected into guinea pigs, following which the animals were bled. The guinea-pig serum, presumably containing bone-marrow antibodies, was injected into rabbits. A single large dose produced an indiscriminate necrosis of all the bone-marrow elements, the blood showing leukopenia and anemia. Repeated small doses caused fibrosis of the marrow.

Dameshek and Wolfson[17] direct attention to the possible beneficial effects of the sulfonamide drugs in combating *agranulocytosis*. Because patients with agranulocytosis do not die of the reduction in granulocytes per se but rather of the resulting secondary sepsis, it was thought that the sulfonamides might be useful in combating the sepsis, the patient's bone marrow meanwhile having an opportunity to recover. Dramatic recoveries occurred in 2 very severe cases of aminopyrine agranulocytosis in which full doses of sulfathiazole were given. It is worth while remembering that the sulfonamides act by bacteriostasis and may be given with impunity in conditions with marked leukopenia.

With respect to the bone marrow, *sternal puncture* as a diagnostic help becomes ever more popular. As Mendell, Meranze and Meranze[18] report, it is virtually diagnostic in acute leukemia, aleukemic leukemia, multiple myeloma, leishmaniasis, malaria and Gaucher's disease. I believe that when taken in conjunction with the blood picture the bone-marrow biopsy is all important in the study of cases of obscure or refractory anemia, and in anemias accompanied with increased hemolysis. Simple puncture is usually satisfactory, and in any event can always be done as a preliminary method. It is only occasionally necessary to resort to trephine biopsy of the sternum, a measure that becomes of value in assessing the general architecture of the marrow tissues, as in aplasia, fibrosis or certain cases with neoplastic infiltration. Shapiro and Bassen[19] report their methods and the results obtained in studying the sternal marrow during the first week of life. They found that the formation of the red cells becomes suddenly curtailed during this period, perhaps because of the better oxygenation present in the outside world.

The *blood volume* in normal infants and children has been studied by Brines, Gibson and Kunkel,[20] using the dye Evans blue and a photoelectric colorimeter. The total volume, about 300 cc. at birth, doubles during the first year of life, and thereafter increases until puberty, when it is about 2500 cc. Both plasma and total volume are more closely related to physical size than to age, and may thus be predicted on the basis of the child's height, weight or surface area to a degree of accuracy sufficient for practical purposes. Some interesting studies on the response of normal subjects to acute blood loss have been made by Ebert, Stead and Gibson.[21] The blood loss was observed under controlled conditions in 6 subjects from whom 760 to 1220 cc. of blood was withdrawn. The decrease in blood volume by hemorrhage was compensated in two ways: by vasoconstriction and by the addition of fluid to the blood stream. The change in hematocrit percentage accurately reflected the direction of the changes in the plasma volume in these experiments. Thus the continued increase in plasma volume was not well shown by a decrease in protein concentration but by a steady fall in the hematocrit reading, since the red-cell volumes remained relatively constant during a period of three days. These findings are important from the standpoint of studying cases of severe

blood loss with or without accompanying shock. The production, utilization and interrelation of hemoglobin and plasma proteins are discussed by Whipple[22] in a review of the fundamental work which has been carried on for years in the famous dog colony and laboratories of the University of Rochester Medical School.

Blood Transfusions and Blood Groups

Owing of course to the exigencies of war, the transfusion of blood and plasma has assumed tremendous importance. By now everyone is familiar with the life-saving qualities of plasma in traumatic, hemorrhagic and surgical shock. Plasma, replacing as it does the fluid lost from the circulating blood, is an urgent necessity. Numerous methods have been published for preparing, storing, freezing, drying and administering plasma. In a series of articles, Strumia, McGraw and Reichel[23, 24] give detailed directions for its preparation and preservation. These writers strongly advocate centrifugation of the blood to increase the plasma yield, and storage of the plasma in a frozen state. They claim that the latter procedure reduces infection to a minimum, and that this possibility may be still further reduced by collecting the plasma from the whole blood within twenty-four to forty-eight hours after its removal. In their fourth paper, the preparation of dried plasma is considered. The latter is of special value because it permits safe and prolonged storage and transportation under adverse conditions, and because the plasma may be reconstituted in a concentrated form for such conditions as edema of the brain. The methods developed by Strumia et al. have been widely utilized.

At the Army and Navy Blood Plasma Division in Washington, headed by Commander Newhouser* of the Navy and Lieutenant Colonel Kendrick of the Army, plasma is stored in liquid form (with added Merthiolate) or kept frozen. Both the liquid and the frozen plasma are shipped throughout the country for use at various Army and Navy posts. Dry plasma, which is prepared by pharmaceutical houses from part of the donated blood, is used only for shipment abroad. Both liquid and frozen plasma have been found eminently satisfactory. Liquid plasma prepared by a *closed method with scrupulously aseptic technic* has been stored for at least twelve months at room temperature. When thus carefully handled, it not only remains free from bacterial contamination but is satisfactory for immediate use in shock. Furthermore, it does not require melting from the frozen state nor reconstituting from the dried product.

Novak[25] recommends the use of one of the sulfonamides, preferably sodium sulfathiazole, in the preservation of blood plasma in a liquid state. A solution of 1.5 gm. of sodium citrate and 1 gm. of sodium sulfathiazole in 50 cc. of normal saline is used for 450 cc. of blood, giving a concentration of sulfonamide of 0.2 per cent. This method has been criticized by some and is not generally accepted.

Crosbie and Scarborough[26] present a series of studies on stored blood, which deal with such matters as the fate of the red cells, leukocytes and platelets, together with prothrombin content, coagulation time and so forth. These factors are also considered by Strumia and McGraw.[27] It is apparent that the drying of plasma results in the loss of almost all the prothrombin and of a portion of the complement present in liquid plasma. Since complement may be of value in combating infection, the use of dried plasma alone, as in burn cases, may not be completely desirable.

Work on the preparation of albumin from human and bovine blood has been vigorously pursued. From the standpoint of osmotic pressure and the retention of fluids within the vascular tree, albumin is of far greater importance than serum globulin. Thus, Newhouser and Lozner[28] have reported that 25 gm. of human albumin is osmotically equivalent to 500 cc. of citrated plasma, provided the patient is normally hydrated. It may be given in a small volume (100 cc.) of solution, and has a greater plasma diluting effect than twice the ordinary 250-cc. unit of plasma. This material, one of the chief advantages of which is its small bulk, is now being packaged for use in the Navy. It is chiefly of value as an emergency first-aid measure and its use has thus far been circumscribed by numerous precautions. At present, it cannot replace whole plasma.

A community method for the collection, preservation and distribution of plasma has been described by Gottlieb and Clapperton.[29] The existing fourteen community hospitals centering about the Central Maine General Hospital at Lewiston are utilized. All the bottles, apparatus and so on are prepared at the central hospital. In the community hospitals, blood is drawn from volunteer donors and is shipped to the central hospital, where it is processed. Part of the plasma is left in a large refrigeration unit at Lewiston, the remainder being returned to the community hospitals. In the event of disaster, the stock of plasma at the central station can be made immediately available for any of the smaller hospitals.

*I am indebted to Commander L. R. Newhouser (MC), U.S.N., for his kindness in verifying the statements relating to the Navy work with blood plasma and albumin.

All the bottles, apparatus and so on are prepared at the central hospital.

The question of the rate of hemoglobin regeneration in blood donors has been studied by Fowler and Barer[30] who found that the average time required to replace 550 cc. of blood was 49.6 days. Some subjects, on the other hand, required three months. With iron therapy, the average recovery time was shortened to 35.2 days. Fowler and Barer suggest that unless hemoglobin levels are regularly determined, an interval of three months between blood donations should be allowed.

The infusion of blood and other fluids via the bone marrow has assumed some importance, since the sternal-marrow space is almost always readily available, at least in adults and older children, whereas veins may at times be inaccessible. Tocantins and his co-workers[31] have demonstrated that substances injected into the bone-marrow cavity are immediately taken up into the venous circulation. The method is particularly applicable in infants and in patients with collapsed veins, as in shock, and when veins are completely inaccessible, as in patients with extensive burns. In infancy, below the age of two, the needle is introduced into either the upper end of the tibia or the lower end of the femur. Fluids, including blood, are introduced either by gravity, or by positive pressure if more speed is desired. For further details of the technics involved, the original papers should be consulted. Tocantins has recommended a special double needle. By the use of a simple sternal-puncture needle,* however, Doud and Tysell[32] administered 9025 cc. of whole citrated blood and 13,950 cc. of fluids to a patient with uncontrollable hemorrhage from the bowel due to ulcerative colitis. The needle remained in situ for several days at a time without evidence of infection or other complication. When blood or fluids were not being administered, the needle stylet was replaced. In this case, the procedure seemed definitely life-saving.

There is some controversy regarding the use of so-called "universal donors" (Group O). Although most authorities now believe that the blood of these donors, because of its content of anti-A and anti-B agglutinins, is inadvisable for use in Group A, B and AB recipients, this is contradicted by others, for example Rosenthal and Vogel.[33] An analysis by these investigators of 819 transfusions with universal donors has shown that such transfusions are not followed by any greater number of reactions than are those with homologous blood. They believe that the universal donor is both reliable and safe for citrate transfusions in emergencies, either in civil practice or in the armed forces. My own experience indicates that in severe anemia, and particularly in hemolytic anemia, it is unwise to use anything but homologous donors. The agglutinin content of the universal donor's blood plasma, although safe enough in ordinary cases, may be high relative to the cells of severely anemic blood, more particularly when spherocytosis is present. Furthermore, in hemolytic cases the possibility of an isohemolysin or atypical intragroup agglutinin is always present.

Hemolytic reactions following transfusions of blood of the homologous group, with particular reference to the Rh factor, are described by Wiener.[34] It is possible to immunize an individual of the same blood group but who is Rh– with Rh+ blood, with the result that he develops an anti-Rh agglutinin. When another transfusion of Rh+ blood is then given, agglutination of red cells takes place within the patient's circulation, with a resultant hemolytic reaction. Wiener advocates that whenever possible, homologous Rh blood be used in repeated transfusions. A safe universal donor, according to this author, is one of Group O, Rh–, with a low titer of isoagglutinins in his serum. To guard against the possibility of an atypical hemolysin or agglutinin, it is necessary to perform careful compatibility tests when repeated transfusions are given. These are done by the Landsteiner–Levine test-tube technic, in which 1 drop of 2 per cent red-cell suspension, 1 drop of serum and 1 drop of saline are incubated at 37° C. for half an hour, following which the mixture is examined both macroscopically and microscopically for agglutination. An ingenious method of utilizing Group O blood for universal-donor transfusions is the addition to the drawn blood of A and B substances, as developed by Witebsky and his co-workers. These substances, carbohydratelike in nature, possess the properties of the A and B agglutinogens and therefore absorb or neutralize anti-A and anti-B agglutinins normally present in Group O plasma. A solution containing the A and B substances is being prepared by a pharmaceutical house for clinical use. Further investigations by Witebsky and Klendshoj[35] have resulted in the isolation of an O-specific substance from gastric juice. This gives additional evidence of the presence of an O agglutinogen, although usually the dictum has been that no such substance is present, and that Group O cells are devoid of both A and B substances.

*Manufactured by the Becton-Dickinson Company, Rutherford, New Jersey, or the Hub Needle Company, Boston.

Pernicious Anemia and Related States

Pathogenetic Mechanisms

The vexing problem regarding the site of origin of Castle's intrinsic factor has been investigated in

the pig by Meulengracht and more recently in the human being by Fox and Castle.[36] Meulengracht assumed that of the various available animals for study the stomach most closely comparable to the human one was that of the pig. He found that in this animal the region of the pylorus (pyloric gland organ) was hematopoietically active, whereas the fundic portion was inactive. In human pernicious anemia, on the other hand, it is the fundic glands that are regularly involved, the pyloric portion remaining histologically normal. Meulengracht then formed the rather striking hypothesis that the fundus acts simply as an initiator or pacemaker of the pyloric-gland region, and that in the absence of this initiator there is no secretion of intrinsic factor. However, as Fox and Castle point out, these pieces of evidence become contradictory "only when conclusions which undoubtedly obtain for the hog are directly translated to man." These investigators demonstrated that extracts made from human stomachs showed very little if any activity in the pyloric region, although marked activity in the fundic regions was present. Thus there is a direct correspondence of the histologic lesions of the stomach of pernicious anemia with the physiologic experiments carried out with human material.

The neurologic lesions of pernicious anemia are often out of all proportion to the extent of the anemia. Conversely, many classic cases with outspoken anemia have minimal neurologic disturbances. This dissociation between the hematologic and neurologic changes has led many investigators to speculate that they may be due to different types of deficiency. Wintrobe and his co-workers have for many years tried unsuccessfully to reproduce in animals the hematologic changes of pernicious anemia. However, in the course of their investigations, the neurologic manifestations have been faithfully reproduced by the use of a diet deficient in various fractions of the B complex, but in which thiamin, riboflavin and nicotinic acid were supplied.[37] Wintrobe's investigations have cast doubt on thiamin as the antineuritic vitamin. In these studies, the neurologic lesions were completely prevented by the use of potent liver-extract preparations given orally and by the use of pyridoxin (B_6), pantothenic acid and perhaps choline. Is the deficiency of these substances then the cause of the neurologic lesions of pernicious anemia? This question and the problem of the exact relation of these studies in swine to human disease remain to be answered. The continued failure of many different groups of investigators to reproduce in animals the typical hematologic disturbances of pernicious anemia suggests either that a deficiency state may produce results in man different from those in experimental animals, or that the concept of the intrinsic factor, its formation, elaboration and so forth is only partially explanatory of the pathogenesis of the disease.

Certain cases of pregnancy are associated with the typical blood changes of pernicious anemia. The gastric analysis may show free hydrochloric acid, and complete recovery may occur after a period of liver-extract therapy. Segerdahl[38] studied the sternal marrow of several cases and found megaloblastic and leukocytic changes as seen in typical pernicious anemia. There can thus be no doubt that a liver-extract deficiency accounts for the development of these cases. Whether this is dietary in origin or due to a large abstraction of material from the mother by the fetus is not clear. Liver extract alone is often only very slowly curative, and transfusions are also required in a few cases.

Not all macrocytic anemia is pernicious anemia. Thus, the macrocytic anemia of hepatic disease, more particularly cirrhosis, does not necessarily indicate that there is a deficiency of the liver-extract principle. In the experience of practically all investigators, purified liver extract produces little if any change in the blood picture. Furthermore, the demonstration by Schiff and his co-workers[39] some years ago that the specific antianemic substance is present in human livers with cirrhosis indicates that the two macrocytic anemias are of entirely different origins. Rarely, pernicious anemia with the typical bone-marrow findings and response to liver extract is coexistent with cirrhosis. Ratnoff and Patek[40] found 2 such patients in their series of 386 well-studied cases.

The blood picture of sprue, both tropical and nontropical, differs in several small respects from that of Addisonian pernicious anemia. The red cells are regularly macrocytic without much change in size or shape, the platelets may be normal, the bilirubin content of the blood is usually low, and so on. Furthermore, free hydrochloric acid is present in the gastric juice of most patients; the bone marrow is hardly megaloblastic in character; there are severe intestinal disturbances, often associated with hypocalcemia; the sugar-tolerance curve is flat; and the response to liver extract is either sluggish or nil.

Hanes[41] describes several cases of the sprue syndrome (including celiac disease and sprue), and Molina[42] describes 100 cases of tropical sprue. Extreme muscular wasting was striking in Molina's cases. Direct examination of the gastric and rectal mucosa showed changes similar to those seen in the tongue and pointed to faulty absorption of food products by the bowel. Although a deficiency state is undeniable, the fundamental cause of the intestinal malabsorption is still obscure. The concept advanced by Castle and Rhoads in 1935 that a deficiency state similar to if

not identical with pernicious anemia is present is questioned by Molina, who points to the severe intestinal dysfunction as the most prominent feature of the disease. This may be due to the continued use of fried or greasy food and of cereals, with resultant irritability of the bowel. The x-ray findings in the small intestine in sprue and in vitamin B deficiency are beautifully described by Golden.[43] A deficiency pattern, centering about changes in the small bowel, is pictured in which the prominent features are hypermotility and later hypomotility, abnormal segmentation, "scattering effect," gas and fluid levels, changes in the mucosal membrane and so forth. These changes frequently respond strikingly to liver-extract or yeast therapy. Further studies along the same lines are presented by Lepore and Golden.[44]

Treatment

A number of experimental studies have recently appeared dealing with further attempts at using the experimental animal for the assay of liver-extract preparations. Several of these studies have dealt with the supposedly megaloblastic, liver-extract-deficient type of hematopoiesis in the embryo. Thus, Stasney and Higgins several years ago used the newborn rat, and more recently Stasney and Burns[45] utilized young opossums, which are conveniently situated (like kangaroo young) in a pouch and yet are embryonic. The changes in the size of the red cells after administration of liver extract has been utilized by these observers as a criterion of response to therapy. Jones[46] used pregnant rats from which eleven-day embryos were obtained. Blood smears of the yolk sac of the embryo were stained and the red-cell and nuclear diameters were counted both in control animals and in those in which the mothers had been given either gastric or liver-extract preparations. The assumption was of course made that the erythrocyte-maturing principle had passed across the placental membrane. Jones demonstrated a definite effect on erythropoiesis in the embryo as indicated by a reduction in the mean cell and nuclear diameters of the primitive erythroblasts. Ventriculin concentrate was most effective. The results of both Stasney and his collaborators and of Jones have been questioned by Last and Hays,[47] who found that statistical analysis of the data indicated that the responses in the treated animals were within the range of biologic variation. They concluded that neither opossum nor rat embryos should be used in the bioassay of antianemia preparations. The mildly polemic postscripts of Jones *vs.* Last and *vice versa* make interesting reading. Further studies by Hays, Last and Koch[48] indicate that erythropoiesis in the three-to-seven-day-old chick embryo also cannot be utilized for assay purposes. For the present, one must still be content with human assay material, which is, however, scarce and often difficult to control.

The striking changes in the bone marrow from a megaloblastic picture to one that is normal (normoblastic) in type are further discussed by Davidson, Davis and Innes.[49] Dameshek and Valentine[50] several years ago investigated the changes that occur and interpreted them as a change from a liver-extract-deficient megaloblastic erythropoiesis to a liver-extract-satisfied normoblastic type. Davidson et al. claim that the megaloblast is not specific for liver-extract deficiency and interpret the rapid changes after treatment as indicative of a normal type of erythropoiesis. My own interpretation of the same phenomena, which is radically different, seems borne out by bone-marrow studies in various other deficiency syndromes.

The clinical use of liver-extract therapy is considered in a group of articles by Evans and Jordan,[51] Strauss, Patek, Pohle, Fox and Burchenal,[52] and Seymour, Heinle and Miller.[53] Evans and Jordan found that a highly concentrated liver-extract preparation (Reticulogen) was far more effective than less concentrated extracts, not only in controlling the blood counts but in improving the neurologic lesions. Strauss and his co-workers, after an initial bias for the very crude extracts, have now adopted a uniform maintenance dose of 15 *U.S.P.* units of purified liver extract every four weeks. During eighteen months of this regimen no subjective or objective relapses in the blood, gastrointestinal or nervous system were observed. Seymour et al. found that patients differed in their ability to store large quantities of liver extract given in relapse. This difference probably depends to great extent on the degree of intrinsic factor lack and to some extent on the diet (that is, the potency of the extrinsic factor).

(*To be concluded*)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29051

A seventy-five-year-old woman was referred to this hospital because of difficulty in swallowing, epigastric discomfort and nervousness.

Twenty-five years before entry, the patient felt a nodule about the size of a walnut on the left side of the neck. Her physician said that her basal metabolic rate was normal and that the nodule had no significance. Thirteen years later, because of a "nervous spell" characterized by headaches, nervousness and mental uneasiness, she consulted a local clinic. At that time there was no sweating, palpitation, tremor or diarrhea and the neck nodule had not increased in size. At this clinic, because of an apparently normal x-ray film of the chest and an unremarkable basal metabolic rate, the patient was told that the neck nodule would never bother her. Five months before entry she noticed that food seemed to stick in her throat, and several days later her neck began to swell. Six weeks before entry, her physician advised an operation on the "goitre," and four weeks later she entered a community hospital. There an x-ray film of the upper chest and neck revealed an "adenomatous goiter" that extended 4 to 5 cm. below the clavicles; the trachea was deviated to the right. The blood cholesterol was 215 mg. per 100 cc., and the basal metabolic rate was −10 per cent. She was treated with a course of x-ray radiation to the neck in five divided doses, following which her neck became swollen. She was referred to this hospital for further care. She had never noticed exophthalmus, palpitation, sweating, tremor, diarrhea, jaundice, abdominal pain or tarry, bloody or acholic stools.

The family and past histories were noncontributory.

Physical examination revealed a dyspneic and orthopneic woman who did not appear to be in great distress. The left pupil was larger than the right, but both were round and reacted to light and accommodation. The thyroid gland was enlarged on both sides, particularly on the left, and extended beneath the sternum; it seemed quite firm, but no discrete nodules were felt and no bruit was audible. The external jugular veins were prominent over it, and the trachea was deviated to the right. The heart was not enlarged, and the sounds were of good quality; occasional extrasystoles occurred, but no murmurs were audible. The examination of the lungs and abdomen was negative. There was fixation of the left vocal cord, and some compression of the infraglottic airway.

The blood pressure was 170 systolic, 90 diastolic. The temperature was 97°F., the pulse 89, and the respirations 24.

Examination of the blood revealed a hemoglobin of 80 per cent and a white-cell count of 7700. The urine was acid in reaction and gave a "green" sugar test and a + test for albumin; the sediment contained 15 to 20 white cells and 1 or 2 red cells per high-power field. The sugar test was "blue" on two subsequent examinations.

An x-ray film of the chest, including the neck, demonstrated a large soft-tissue mass occupying the position of the thyroid gland, measuring 10.5 cm. across and extending substernally to the level of the aortic arch. The mass was of considerable density. The chest was narrowed laterally. The diaphragm was low in position and showed limited motion on both sides. The lung fields were unusually bright, and there was an increase in the markings. The heart was small. An electrocardiogram demonstrated a normal sinus rhythm of 90. The PR interval was 0.14 second; the T wave was isoelectric in Leads 1, 2 and 3, and T_4 was shallow; the ST segment in Leads 2 and 3 was slightly depressed.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. SAUL HERTZ: I should like to emphasize that the patient found the nodule and went to her physician. I think the lump that the patient finds is probably more significant than the one that the doctor finds. For a patient to remember twenty-five years back is an important point in the diagnostic elements of the case. The physical examination later describes a uniform enlargement in the region of the thyroid gland and that is why I am making this point about the patient's description of the nodule. Apparently the physicians in the clinic that the patient visited found the same thing and confirmed the patient's finding.

We are not certain whether it was truly the thyroid gland that was involved. The fact that she was treated with x-ray radiation seems to indicate that her physicians were thinking of lymphoma, and gave a therapeutic x-ray trial, apparently without a biopsy. The swelling after x-ray therapy might point to some form of lymphoma,

but I do not believe that is a significant point in the differential diagnosis; however, the lack of response is.

We are left, then, with an old lady with a twenty-five-year-old mass in her neck, which apparently had undergone certain changes in the previous twelve years, particularly in the previous five or six months. On physical examination, dyspnea and orthopnea were found in a person who was described, nevertheless, as not being in great distress. Orthopnea may not be distressing for some people, but I am sure it would be for me. One would like to know whether they thought the orthopnea was associated with definite stridor. That would be important in ascertaining the degree of compression of the trachea and would help quite a bit.

The dilatation of the pupil on the left indicates stimulation of the cervical sympathetic nerves on that side. It seems to indicate disorder in the left lobe of the thyroid gland, if it was the thyroid gland, compressing the recurrent laryngeal nerve and causing paralysis of it. We are told later that the vocal cord on that side did not move.

The description of the gland is of value in trying to diagnose this case. I should like to be sure that it was uniformly enlarged and non-nodular, because it makes all the difference in the world in defining this case as cancer of the thyroid or chronic thyroiditis. A picture similar to this can be produced by the invasive type of chronic thyroiditis, Riedel's struma, causing involvement of the recurrent laryngeal and sympathetic nerves. Apparently there was also some interference with venous circulation, pointing to an upper mediastinal syndrome, conceivably on a lymphomatous basis.

The deviation of the trachea to the right is significant because it tends to indicate that the disease was well defined on the left and possibly that the old nodule had something to do with the recent disorder. In the past history of cases of thyroid cancer, the finding of pre-existing goiter is frequent.

The invasive character of the mass in the neck is in favor of either carcinoma or chronic thyroiditis; although a nontoxic goiter that has expanded because of hemorrhage or cystic degeneration may cause considerable pressure on the recurrent laryngeal nerve and give a picture similar to this, I think it unlikely.

At the age of seventy-five, with a nodule of many years' duration, which I am taking seriously, carcinoma has to be considered as the first possibility. However, the fact that the thyroid gland is described as uniform makes me lean toward chronic thyroiditis. I think the x-ray film will be helpful and should like to see it at this point.

DR. LAURENCE L. ROBBINS: This is the mass that lies in the region of the thyroid gland. It is practically symmetrical on both sides, and extends down to the level of the aortic arch. I notice that the report said that the mass was of considerable density. They probably meant ordinary soft-tissue density. I do not believe that there are areas of calcification within the mass; there is a fleck here but it is probably pleural or in the lung. The remainder of the chest shows considerable emphysema and questionable early fibrosis.

DR. HERTZ: The x-ray film suggests that the mass was uniform. I cannot remember having seen a case of chronic thyroiditis in which the mass extended into the thorax to this extent, and I tend to rule it out on that basis. That brings me down to one diagnosis — thyroid carcinoma in a long-existing nodular goiter. There are a few rare conditions that should be considered. Could this be something other than the thyroid gland, even though the x-ray man and the clinical examiners indicated that the thyroid gland was involved, and the early story centers around the thyroid nodule? Perhaps the unusual turned up here, and I should like to put on record the possibility of carcinoma of the esophagus or bronchus, since the patient complained of dyspnea. But I doubt whether these would cause metastasis to the mediastinum of this type without more characteristic glandular metastasis in the neck. If this was an extrathyroid cancer it manifested itself in an odd way. There is also a bare but unlikely possibility that this was a benign tumor, a nontoxic nodular goiter.

CLINICAL DIAGNOSES

Tracheal obstruction, due to colloid goiter.
Arteriosclerotic heart disease.

DR. HERTZ'S DIAGNOSIS

Carcinoma of thyroid.

ANATOMICAL DIAGNOSES

Malignant lymphoma, stem-cell type, of cervical and mediastinal nodes.
Nodular colloid goiter.
Tracheotomy.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Shortly after entering the hospital the patient developed symptoms of marked respiratory obstruction; it was believed that emergency relief was required so a tracheotomy was done and a small portion of the mass was removed, in part as a biopsy and in part with the hope of relieving some of the tracheal obstruction. Microscopic examination showed a benign colloid goiter. Following the operation, the patient ex-

perienced little relief and had successive episodes of severe tracheal obstruction, some of which could be relieved by aspiration of the tracheal secretions; she eventually died with respiratory obstruction.

The autopsy showed a large tumor mass in the upper mediastinum and lower neck that completely encircled the thyroid gland but did not involve it. This turned out to be a malignant lymphoma of the undifferentiated or stem-cell type. The thyroid gland was only slightly enlarged, and we did not find any particular area that we were convinced was the mass the patient had noted for twenty-five years. That must have been lost in the general tumor mass.

DR. HERTZ: I want to emphasize one point. We are often asked what to do about a single nodular goiter. Frequently the history is given that the patient has had such a mass for twenty or more years. Here is a case in point. How much can we trust the history in dealing with nontoxic nodular goiter? It is of no great diagnostic value to us unless we have seen the nodule ourselves and have made up our minds that it did lie within the thyroid gland. But nothing is said in the record whether the mass rose and fell after deglutition, an observation that should be recorded in any description of a case where the possibility of thyroid disease is considered.

DR. MALLORY: I think that all the examiners felt quite sure that it was thyroid gland, including the surgeon who operated on her, who still thought the obstruction was due to the goiter when the operation was over.

CASE 29052

PRESENTATION OF CASE

A fifty-nine-year-old widowed housekeeper entered the hospital because of a vague epigastric distress that often interfered with her sleep.

During most of her adult life the patient had, like her mother before her, suffered with brief attacks of "biliousness" that occurred once or twice each year and spontaneously disappeared. Occasionally during these episodes she vomited small amounts of green, bitter fluid and had shaking chills. Four months before entry vague epigastric distress developed and often interfered with her sleep. The discomfort bore only a questionable relation to meals and was not relieved by soda. At no time did the vomitus contain blood or coffee grounds, and she never had diarrhea, constipation, jaundice, melena or weight loss. Nine days before admission a physician felt an egg-sized lump in the abdomen and advised hospitalization.

The family history was noncontributory. The menopause had occurred seven years before entry, and the uterus was removed because of fibroids three years later.

Physical examination revealed a sallow, middle-aged woman in no distress. The examination of the heart was negative. A few crackling rales that did not disappear on coughing were audible at the base of the right lung. In the upper midepigastrium just below the xiphoid there was an egg-sized, firm, rounded, slightly tender mass that was quite movable, descended only slightly with respirations and seemed to pulsate.

The temperature was 98.9°F., the pulse 81, and the respirations 19.

The urine was negative. The blood Hinton was negative. A barium meal revealed a normal esophagus. There was a pressure defect on the lesser curvature of the stomach in the region of the angle; this was due to extrinsic pressure, and there was no evidence of intrinsic disease. The duodenal loop was not remarkable. At the end of six hours the barium lay on the proximal colon.

On the fourth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ERNEST DALAND: This patient's symptoms really date back four months although there were indefinite symptoms before that. She had had no vomiting of blood or coffee-grounds material, suggesting that her difficulties had no intrinsic relation with the stomach. There was no diarrhea, constipation or jaundice, which is important. She had had a hysterectomy four years before entry. It is presumable that the operator passed his hand around the epigastrium at the time of operation and that this mass was not there at that time. An egg-sized, firm, round, slightly tender mass was felt at this admission. Those of you who have operated on an extensive cancer of the stomach that has not been felt beforehand must have been impressed with the size of a tumor that can be hidden in the epigastrium without being palpable. Here we have an egg-sized mass that the local physician felt, and also the man on the ward.

The first thing one would have to think of is an epigastric hernia. There is no note whether there was any impulse on cough, but many times in an epigastric hernia there is no impulse. However, as we go on and find that the x-ray films showed a pressure defect on the stomach I think we can rule out anything in the abdominal wall. There was something within the abdomen.

I should like to see the x-ray films. The number of structures that we have to consider in this region are distinctly limited. The left lobe of the liver may sometimes be palpated but would not be picked up as an egg-sized mass. The pancreas is

located here, as well as the stomach wall, the lymph nodes along the lesser curvature and the aorta. These are the organs that we have to consider.

DR. MILFORD D. SCHULZ: This I believe is the defect caused by the extrinsic mass that was described. You can see that the rugal folds pass uninterrupted over the area. The same is true in this spot film, which confirms the opinion of the fluoroscopist that this was an extrinsic mass. I think we might note that there is no evidence of erosion of the vertebras so far as can be seen on these films.

DR. DALAND: Might it be something in the stomach wall and still have the rugae normal without ulceration?

DR. SCHULZ: Yes; but you would expect to see some displacement of the folds as they pass over the mass in the stomach wall. If it is intramural, there is usually some point of ulceration.

DR. TRACY B. MALLORY: However, myomas can be pedunculated and hang externally and not necessarily show any thickening of the stomach wall.

DR. SCHULZ: Yes; but then it often shows some evidence of tug on the stomach.

DR. DALAND: First is the question of aneurysm. The mass was said to be pulsating. There is no note whether there was any bruit on stethoscopic examination, or whether there was any expansile pulsation. There are no lateral films. A lateral film would probably have been taken if they had a strong suspicion of aneurysm, since it might have demonstrated erosions of the vertebras that could not have been seen in the anteroposterior view. I think we can discount the possibility of aneurysm. In this plain film there is a shadow. Is it a mass?

DR. SCHULZ: It is rather indefinite.

DR. DALAND: I was given permission to look at these films before the conference and that was the only suspicious thing that I saw.

DR. SCHULZ: Of course, it could be a mass.

DR. DALAND: The pancreas is the next thing to be considered — a cyst of the pancreas or a tumor of the pancreas. Ordinarily, pancreatic cysts are in the loop of the duodenum — that is, if they arise in the head of the pancreas. However, the pancreas does extend across the midline at about this point and it would be possible for a cyst of the pancreas to present here; a lateral view would help a good deal in deciding whether the stomach was pushed forward. I thought tumor of the stomach wall was a definite possibility; a benign leiomyoma of the stomach wall which had been there for some time might produce this picture. A malignant leiomyosarcoma would probably have ulcerated by this time and would give a defect on the inside of the stomach. The commonest tumor of the stomach next to carcinoma is leiomyoma, and I think that that is a decided possibility.

The other possibility is lymphoma. Such a tumor may occur in any place where there are lymph nodes, and this is a suitable location. There is no evidence of lymphoma anywhere else, and since the difficulty had apparently been going on for four months, I think that if it had been lymphoma there would have been other evidence of the disease.

I believe that this was a cyst of the body of the pancreas.

DR. FRED A. SIMMONS: I assisted at the operation on this patient. The houseofficer was given his choice of diagnoses after having had the privilege of palpating the abdomen under anesthesia; he chose pancreatic cyst. I was given a choice and chose leiomyoma of the stomach. The surgeon with his mature judgment said hydrops of the gall bladder. The mass was definitely to the left of the midline and larger than an egg, being 10 cm. long and 5 cm. broad. It was hard, movable and not adherent.

CLINICAL DIAGNOSIS

Hydrops of the gall bladder?

DR. DALAND'S DIAGNOSIS

Cyst of body of pancreas.

ANATOMICAL DIAGNOSIS

Hydrops of gall bladder.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was explored and an enormous gall bladder was found, which crossed anterior to and above the stomach, producing a pressure defect on the lesser curvature. When finally explored, it turned out to be even bigger than it seemed under anesthesia. It was 15 cm. in length and nearly 10 cm. in diameter, and it contained clear mucinous fluid and a considerable number of stones. I also called it a pancreatic cyst when I read the record, Dr. Daland. A lateral x-ray examination would probably have told the story.

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THE LABORATORY IN WARTIME

Now that medical personnel has been heavily depleted for the needs of the armed services, it becomes increasingly important that the practitioners still caring for the civilian population be able to carry on the work they do with the highest degree of efficiency.

An important factor in diagnosis and in the control of treatment is the information made available by the laboratory. The aid that a positive serologic reaction for syphilis may give in unraveling a diagnostic puzzle is as striking as the information that roentgenologic examination gives to the surgeon in a case of fracture or that hematologic studies afford to the internist studying a case of pernicious anemia or leukemia. Hardy is the surgeon who trusts to his gross examination of a removed lesion to determine whether malignancy is present.

One of the striking developments in medicine of the past two decades has been the phenomenal expansion of the use of the laboratory. Laboratory procedures have opened up new investigative technics and have done much to simplify the understanding of many pathologic processes. So much can be done by the laboratory that it has sometimes received an unfair share of the diagnostic burden. Fifteen years ago the determinations of blood-sugar levels, of sedimentation rates and of the amounts of serum protein were more or less rarities; but today, fortunately, they are matters of everyday performance and a requisition slip sent to the laboratory elicits prompt information concerning the desired test.

These laboratory procedures have different degrees of usefulness, and the complexity and reliability of the tests also vary to an appreciable degree. Such tests as the number of white cells, the amount of hemoglobin and the level of nonprotein nitrogen in the blood may be carried out with great accuracy and dispatch. On the other hand, methods such as the hippuric acid test for liver function and the test for serum amylase may be neither accurate or informative.

Although it is easy in most hospitals to requisition any amount of laboratory work, all too often these studies are demanded without regard to the clinical condition of the patient and without any clear idea of what positive information may be obtained and what are the limitations of the tests. Much laboratory work that is useful under a certain set of circumstances is valueless or of academic interest under others, and it is worth while for the physician to check over his written orders from time to time to make sure that he really gets significant and useful information from the laboratory. Thus, several years ago pneumococcal typing was of great importance as an emergency procedure. Now, with the widespread use of the sulfonamides typing is unnecessary except in those cases in which serum therapy is also used.

Laboratories have suffered by the loss of pathologists and by the loss of technicians, and a curtailment of the scope of their work is inevitable. If their important help is to be utilized to best advantage, it is essential that there be discrimination by the practitioner in the laboratory tests that he requisitions. Thus, the performance of a complete blood count is undoubtedly of some interest in every patient seen. Unless there is some clinical indication to the contrary, however, a hemoglobin determination is all that is actually necessary, and if it proves abnormal, this serves as a starting point for further investigation. Similarly, a serologic test for syphilis is desirable for every patient, but there is rarely need for this request to be accompanied by one for gonococcal complement fixation and typhoid, paratyphoid and undulant fever agglutination.

Another waste in laboratories is the performance of scattered tests at frequent intervals. Many tests are not of an emergency nature. It is most conserving of laboratory personnel and material if several such tests can be done at the same time, even though it entails two or three days' delay. In this group fall such tests as the determination of blood calcium and phosphorus, of blood cholesterol, and of serum phosphatase.

It also behooves each pathologist to check over the work done in his laboratory, to make sure that there are no ways overlooked in which the available material and personnel can be used to better advantage. Even the tissue pathologist might well consider whether the lengthy microscopic descriptions that take his time to dictate, the secretary's time to typewrite and the surgeon's time to read are really worth the effort and give enough additional information to justify their retention in place of the microscopic diagnosis alone.

All too often in these days it is difficult to get adequate laboratory work done for the patient outside the hospital, and it is almost impossible for the physician to have a technician in his own office. Fortunately, several private laboratories and some hospital laboratories are available for the carrying out of essential laboratory tests for such patients. It might be well worth while for all hospital administrators to consider making available the laboratory facilities of their hospitals, so far as it is possible without impairing efficiency, to those practitioners who find themselves in need of data the laboratory can supply.

SAFE DELIVERANCE

A NEW book by a Boston physician, Dr. Frederick C. Irving,* deserves special attention.

The text is divided into three sections. The first is an autobiography of the author, written in an engaging style. There is much of interest in the account of his early life, particularly regarding his grandfather, a physician who practiced in northern New York, served through the worst battles of the Civil War and passed on his enthusiasm for medicine to his grandchild. Dr. Irving has paid a fine tribute to a man of character and makes one realize that many of the best things in medicine are not entirely due to the great advances in recent years — character in a physician is still a primary and necessary asset. Then come reminiscences of life in Harvard College at the turn of the century and of teaching at Harvard Medical School. The chapters on experiences at the Boston Lying-in Hospital on McLean Street are of great interest, and no one except the inimitable "Fritz" Irving could tell the story as he has done it. There are descriptions, too, of his period as a house pupil at the Massachusetts General Hospital, of which those dealing with the life in the hospital itself and with sidelights on Maurice Richardson and other surgeons are of particular interest. After a brief interval of war service, Dr. Irving returned to this country in 1919. He first assisted Dr. Franklin S. Newell and later succeeded him as chief-of-staff at the Boston Lying-in Hospital and professor of obstetrics at Harvard Medical School.

The second part of the book concerns the history of the Boston Lying-in Hospital, beginning

*Irving, F. C. *Safe Deliverance*. 308 pp. Boston: Houghton Mifflin Company, 1942.

in the earliest days of its existence, more than a hundred years ago, under the guidance of Walter Channing. To him are credited two outstanding contributions to medicine — his description of the anemia that occasionally complicates pregnancy and, of more importance, his introduction of anesthesia in childbirth. Here the story is especially well done, and each chapter is full of enlightening and often amusing anecdotes. Channing was followed, after an interval, by David H. Storer and later by his son, Horatio R. Storer. Both were outstanding obstetricians and contributed greatly to the knowledge of the art. The watchword of the first Storer, "Patience and expectancy up to the proper time for interference: prompt and fearless action when that time comes," should, as Dr. Irving notes, adorn the walls of every delivery room and lying-in chamber. To the second Storer should go the credit for the first operation to remove the uterus at the time of cesarean section, performed in 1868, eight years before the classic monograph by Porro, of Milan. Storer, like Long in the ether controversy, failed to realize the significance of what he had done, and his contribution was lost in the passing of time. Later came William L. Richardson and a host of others who kept the name of the Boston Lying-in Hospital at the front in the advancement of obstetrics in America.

Finally there are chapters on general topics: puerperal fever and the importance of Oliver Wendell Holmes's contribution to the subject, first published one hundred years ago this April; the matron of the hospital, Mrs. Higgins, who served from 1873 to 1914; midwifery in general; abortion, therapeutic and otherwise; puerperal convulsions; cesarean section; legitimacy; and the modern practice in obstetrics.

Throughout the book are notes on the teaching of obstetrics in Harvard Medical School and, indeed, important contributions to general knowledge concerning the teaching of the whole subject of medicine. There are many quotable passages: for example, "The most effective teacher is not the colorless intellectual virtuoso who today deals out as a fact what tomorrow may prove to be only a fancy, or who pursues some petty experimental project; but he is the real doctor who transmits to his pupils the heritage of truth, courage, and kindness that will make his spiritual heirs worthy members of the medical profession."

The book is carefully written and surprisingly full of factual historical material, while enough lightness is given on each page so that a layman may read with both understanding and pleasure. The omission of an index cannot be overlooked, and a chronological tale of events and persons connected with the Boston Lying-in Hospital as an appendix would have greatly aided the average reader.

This is one of the best autobiographies of a doctor published in recent years. Every physician in New England will be delighted with the story unfolded by Dr. Irving. There is plenty of local color, and occasionally a pungent statement, but nothing at any time that will raise a blush in the most fastidious cheek. To the physician outside of the sphere of events ordinarily encompassed by the Boston Lying-in Hospital, this book will be welcome, for in it he will find a rich store of wise comments by a man of broad vision, particularly interested in life, and at the same time a practical, earnest, up-to-date leader of medicine.

MEDICAL EPONYM

Steensen's Duct

Niels Steensen (1638–1686) was born a Danish Protestant, studied medicine, gave up scientific investigation at the age of thirty-five, and died a Catholic priest at the age of forty-eight. He wrote under the Latinized form of his name Nicolaus Stenonis, and is often called Steno under the misconception that this is the nominative form of the supposed genitive Stenonis. The following account of his discovery of the parotid duct is taken from a letter to Thomas Bartholin, dated Leyden, April 22, 1661, and appears in the first volume of Nicolai Stenonis *Opera Philosophica* (Copenhagen, 1910: pages 3–7). The discovery was made in Amsterdam on April 7, 1660, while Steensen was a pupil of Gerard Blaes, director of the Town Hospital. A portion of the translation follows:

It is now a year since I, having become the recipient of Blasius's hospitality, and marking in that acquaintanceship — to which he put an end the third week after my arrival — a convenient opportunity for studying anatomical subjects, begged the famous man to allow me to dissect with my own hand whatsoever things I should be able to gather together for myself. Having obtained this permission, I was so favored by fortune that in the very first thing which I began to dissect alone — a sheep's head that I had bought at Muscolus on April 7 — I discovered a duct which, so far as I know, had never yet been described by anyone. I had removed the usual covering layers and was contemplating the dissection of the brain, when by chance I decided to examine first the vessels of the mouth. And so, to this end exploring the courses of the veins and arteries by inserting a probe, I noticed that the point, when driven but a short way in between the narrow layers, wandered around quite freely in a spacious cavity, and soon, when I pushed the metal probe farther, I heard the sound of it against the teeth themselves.

Struck by the novelty of this, I summoned my host to hear what he thought about it: he first began to accuse me of using force, then to resort to the explanation that it was one of Nature's many tricks, and finally turned to consult Wharton. But he could find nothing there either: and since the carelessness with which I had treated the vessels did not allow a more extensive examination, I resolved to repeat this investigation with greater care; and this I did a few days afterward, using a dog's head, although the results were not so clear. Since, therefore, the use of the vessels was proved by the similarity existing between large and small, I sent word in that same month to my close friend, the excellent Master Jacob Henry Paul, telling him that I had found a certain salivary vessel, and appending thereto some sort of description of it. Since, however, I knew that something similar to this had already been previously discovered, and was unable to learn whether or not it was the *same* thing that had been noted by others, I kept silence, until an opportunity presented itself to consult the great Sylvius on the matter. He, on learning my story, resolved to conduct an investigation, using a human body, and finding my story to be true, demonstrated it on numerous occasions in the presence of observers.

You have here, illustrious Sir, the history of the discovery. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Analysis of Causes of Maternal Death In Massachusetts during 1941

Miscellaneous

During 1941 there were two fatal cases of pernicious vomiting. One of these was that of a woman who had two living children. In this, her third pregnancy, she reported first to her physician six weeks after the last period. At that time she had severe vomiting. She was treated at home for ten days with some improvement but was finally sent to the hospital because of a return of the vomiting. The blood pressure on admission was 90 systolic, 60 diastolic, and the pulse 130. The urine contained large traces of albumin. The patient was jaundiced. For ten days she was treated conservatively, but continued to go downhill; at the end of that time the nonprotein nitrogen was 117 mg., and the urea nitrogen 51 mg. per 100 cc. A consultation was held, and an abortion was advised; but so far as can be made out from the record, the patient died without operative interference. It is difficult to understand how a patient could, under such close medical care as this, have been allowed to die without operative intervention unless certain scruples contraindicated this procedure. Medically speaking, this was an entirely unnecessary death.

The second patient was a twenty-four-year-old primipara, who at the beginning of the pregnancy apparently had a pyelitis. This was treated in a hospital and cleared up. Excessive vomiting, described as pernicious, developed, and abortion was advised. Abortion was accomplished by packing the cervix. The entire fetus was expelled spontaneously. The temperature rose to 104°F. that evening, and the patient died within forty-eight hours of delivery. As fever developed the night following the operation, it was apparent that the operation was the cause of the infection. No autopsy was obtained, but one can attribute this unnecessary death solely to infection following an operation for pernicious vomiting.

There were two cases in which shock and, probably, hemorrhage were responsible for death. The first was that of a patient who had had one early miscarriage. The second pregnancy was normal in its prenatal course. The patient had a rather long labor. Delivery was accomplished, after forceps had failed, by version and craniotomy. The patient lived about an hour after delivery. There was no transfusion. There is little to be said about this case except that it was handled poorly and that the patient should undoubtedly have had a cesarean section. When one has to resort to version, because forceps-delivery is impossible, it is evident that a mistake has been made. And although there was considerable bleeding in this case, the prolonged operative procedure undoubtedly caused the shock that resulted in death.

The second case was that of a multipara who had three living children. She entered the hospital because of a mild hydramnios and albuminuria. Labor was induced with castor oil and rupture of the membranes, but did not proceed satisfactorily. It is evident that the cervix had not softened and was not amenable to induction by this method. After twenty-eight hours of labor a Waters's extra-

peritoneal cesarean section was done because it was believed that a Bandl's ring had formed. The baby weighed 10½ pounds. The patient was transfused eight times but died four hours later of hemorrhage and shock.

Two patients died of cerebral hemorrhage. On one of these the history is incomplete. At seven months it is said the patient had a cerebral hemorrhage and succumbed undelivered. The second patient had been treated for hypertension for two years. When eight months pregnant a cerebral hemorrhage resulted in paralysis of the right side. She was admitted to the hospital and died three weeks later, undelivered. A post-mortem cesarean was immediately performed, and a 5-pound living child was secured. The only sure way to have eliminated this fatality was to have prevented pregnancy.

There were two cases in which, after investigation, the direct cause of death could not be determined. The first case was that of a woman who had had six previous normal pregnancies; the children were living and well. When seven months pregnant, while at a children's clinic, she fainted and was unconscious for an hour. She was immediately sent to the hospital in extreme shock. There was no bleeding and no abdominal spasm; the pulse was 150; no fetal heart could be heard. She started labor ten hours later and delivered a stillborn baby. Since there was no hemorrhage or excessive clots associated with the birth of the baby, premature separation of the placenta can be ruled out. During convalescence she vomited frequently but gradually improved. Suddenly an attack similar to the initial attack, with unconsciousness and pain in the epigastrium, occurred, from which she did not recover. Unfortunately, no autopsy was performed. Because of the rapid pulse and because of the pain in the abdomen and vomiting, it seems likely that a viscus ruptured. The second case was that of a woman in her fourth pregnancy who had had three previous cesarean sections. This pregnancy was terminated by a cesarean section at term. Spinal anesthesia was given. A minute after pituitary extract had been given, the patient had difficulty in breathing and a tickling in the throat. She suddenly became pulseless, and no blood pressure could be obtained. The pulse returned, but an hour and a half later, laryngeal spasm developed and she again became pulseless. Death followed almost immediately. No autopsy was performed, but it is possible that a hypersensitive response to pituitary extract was the cause of this catastrophe.

There were two cases of suicide. In one of these, the patient at term, arrived at the hospital dead; she was at term but not in labor. The cause of death was ascertained to be poisoning from drugs. The second case occurred in a primipara, who shot herself through the head, undoubtedly while mentally deranged.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1942

Diseases	November 1942	November 1941	Five-Year Average*
Anterior poliomyelitis	2	10	5
Chicken pox	969	1172	1035
Diphtheria	6	14	16
Dog bite	583	687	626
Dysentery, bacillary	30	46	48
German measles	62	59	39
Gonorrhea	378	332	422
Measles	1073	456	635
Meningitis, meningococcal	13	14	6
Meningitis, other forms	6	7	†
Mumps	639	692	370
Paratyphoid infections	7	5	5
Pneumonia, lobar	234	193	264
Scarlet fever	883	734	486
Syphilis	535	389	455
Tuberculosis, pulmonary	239	199	200
Tuberculosis, other forms	20	23	21
Typhoid fever	0	2	6
Undulant fever	0	5	4
Whooping cough	955	710	626

*Based on figures for preceding five years.

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

Actinomycosis was reported from: Springfield, 1; total, 1.

Anterior poliomyelitis was reported from: Fitchburg, 1; Lynn, 1; total, 2.

Anthrax was reported from: Lynn, 1; total, 1.

Diphtheria was reported from: Boston, 2; Lowell, 3; Springfield, 1; total, 6.

Dysentery, bacillary, was reported from: Cambridge, 1; Camp Edwards, 1; Fall River, 5; Waltham (Walter E. Fernald State School), 5; Wrentham (State School), 18; total, 30.

Encephalitis, infectious, was reported from: Everett, 1; total, 1.

Malaria was reported from: Camp Edwards, 1; Middleboro, 1; total, 2.

Meningitis, meningococcal, was reported from: Boston, 2; Cambridge, 1; Camp Edwards, 1; Dracut, 1; Fort Banks, 2; Lowell, 1; Milton, 1; Norwood, 1; Randolph, 1; Stoneham, 1; Wilmington, 1; total, 13.

Meningitis, other forms, was reported from: Boston, 1; Cambridge, 3; Fitchburg, 1; Worcester, 1; total, 6.

Paratyphoid infections were reported from: Boston, 2; Lowell, 1; Newton, 2; Salem, 1; Worcester, 1; total, 7.

Septic sore throat was reported from: Attleboro, 4; Beverly, 1; Boston, 3; Braintree, 1; Fall River, 1; Fitchburg, 1; Quincy, 2; Worcester, 1; total, 14.

Trachoma was reported from: Boston, 1; Norwood, 1; total, 2.

Typhus fever was reported from: Camp Edwards, 1; total, 1.

Although the usual high seasonal levels characterize certain of the communicable diseases for November, there were two outstanding exceptions. Typhoid fever, for the first time since the disease was made reportable, is conspicuous by its absence, no cases having been reported during November. Undulant fever, too, was not reported.

No disease reached a record-high figure during the month, but the following exceeded their respective five-year averages: German measles, measles, meningococcal meningitis, mumps, paratyphoid infections, scarlet fever, syphilis, pulmonary tuberculosis and whooping cough. Three of these, measles, scarlet fever and whooping cough, appear to be tending toward even higher levels.

Falling below their five-year averages were anterior poliomyelitis, bacillary dysentery, chicken pox, dog bite, gonorrhea, lobar pneumonia and tuberculosis, other forms.

Diphtheria was reported at a record-low figure.

One case of animal rabies was reported from a city in the north Metropolitan Area.

NOTE

On January 21, Dr. Fuller Albright, assistant professor of medicine at Harvard Medical School, delivered the fourth of the current series of Harvey Society Lectures at the New York Academy of Medicine, the title being "Studies on the Pathologic Physiology of Cushing's Syndrome."

CORRESPONDENCE

COMMISSIONS FOR NONMEDICAL TECHNOLOGISTS

To the Editor: The Army of the United States is looking for medical bacteriologists, medical entomologists, medical biochemists and parasitologists, to be commissioned as first lieutenants in the Sanitary Corps.

Because of the urgent need for these men, the War Department has waived the minimum age limit of thirty-five years for commissioning directly from civil life, and the restrictions against commissioning men in Classes I and II of the Selective Service classification have been removed. Consequently men will be considered regardless of age or draft status. Men who can pass a "limited service" physical examination are acceptable.

The requirements call for college graduation and at least four years' professional experience. Men having degrees of M.A. or Ph.D. in their respective fields may substitute these degrees for part of the experience requirements. Men with medical degrees are not desired under these requisitions, inasmuch as their purpose is to obtain nonmedical men, owing to the scarcity of physicians.

All candidates are requested to communicate with this office.

ELLERTON J. BREHAUT, Major, A.U.S.
Assistant Chief of Branch

Officer Procurement Branch
Headquarters First Service Command
80 Federal Street
Boston

FILING OF BIRTH CERTIFICATES

To the Editor: It has been brought to the attention of the Board of Registration in Medicine that many physicians in the Commonwealth are delinquent in filing birth certificates. At this particular time we all realize how important satisfactory birth certificates are. The Board of Registration in Medicine requests that all physicians file birth certificates promptly and correctly.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Neurology. By S. A. Kinnier Wilson, M.D., D.Sc. (Edin.), F.R.C.P. Edited by A. Ninian Bruce, F.R.C.P. (Edin.), D.Sc. (Edin.), M.D., F.R.S. (Edin.). Two volumes. 8°, cloth. Vol. 1, 751 pp., with 114 illustrations and 117 plates. Vol. 2, 1085 pp., with 217 illustrations and 73 plates. Baltimore: The Williams and Wilkins Company, 1940. $21.00 for the set.

For many years, it has been known that Dr. Kinnier Wilson was working on a two-volume textbook on neurology that would bring the subject up to date. This extensive undertaking was not quite finished when Wilson died unexpectedly. The enterprise, however, was so important that it was felt inadvisable to allow it to lapse, and Wilson's friend and collaborator, A. Ninian Bruce, finished the editorial supervision and saw the work to the press.

Although dated 1940, the book covers a period through 1937–1938. In scope, it is by far the most extensive book on neurology that has been projected in modern times by a single author. It can only be compared with the great book by Oppenheim, which went through many German editions and was translated into English years ago. The value of Wilson's book lies in the completeness of the material and in the references to the literature. No literature of importance seems to have been missed, and what is more, Wilson evaluated each contribution to the subject and only refers to those of importance. The bibliography is therefore selective, and since it was chosen by one of the leaders in neurology, one may assume that poor, unreliable work has been omitted. Wilson certainly read each contribution with great care, and for this feature the book is of outstanding value. In addition, he supplemented his wide knowledge of literature with a long, clinical experience and acute observations of neurological conditions. The book therefore takes its place as the leading text on the subject. The literature has now become too vast for any individual to encompass, and Wilson's book may be looked on as the last great single-author textbook on the subject. It is a worthy successor to the book by Gowers and the even greater compilation by Oppenheim.

No neurologist could possibly be considered as having a library of importance without Wilson's book on the shelf, and indeed, it should be on his desk for daily use. Every medical library and hospital should consider this book as a "must" item, for it at once achieves a position as a standard, definitive text, supplanting any other that has preceded it.

Sex Fulfillment in Marriage. By Ernest R. Groves; Gladys Hoagland Groves; and Catherine Groves. Introduction by Robert A. Ross, M.D. 8°, cloth, 319 pp. and 5 plates. New York: Emerson Books, Incorporated, 1942. $3.00.

Many books on adult sex education for the intelligent layman have recently appeared. This is no better and no worse than the average. Yet one has a right to expect that it should be better, since the senior author, a professor at the University of North Carolina, has lately been publishing every year or two a popular-style book in this field. It can be said to his credit that he has gained in courage and in the accuracy of his reporting on sex subjects.

The questions raised (and answered) are more likely to be in the minds of those living in the more unenlightened areas of the rural South than in the minds of the

sophisticated young people educated in the cities of the North. This is not to say the latter will not learn new facts or gain in judgment by perusing this volume — they will. But it indicates the type of audience for which the book will be most useful. Too many straw men are erected for the fun of knocking them down.

The book comprises twelve chapters: "Importance of Sex," "Experiences That Influence Sex," "Courtship," "Anatomy and Physiology of Sex," "Starting Marriage," "Sex Role of the Husband," "Sex Role of the Wife," "Common Marital Problems," "Sex Hygiene," "Birth Control," "Pregnancy and Childbirth" and "The Larger Meaning of Sex"; there is an ultrabrief bibliography of fourteen books, courageously and well chosen. Although the discussion of birth control leaves much to be desired, it is probably the most accurate and forward-looking account that the senior author has written on the subject. The index is very inadequate, and the introduction seems somewhat "puffy."

The style has the merit of simplicity, but lacks directness. It is verbose even for its audience. There is too much circumlocution. For example, a whole page is devoted to making the point that a man should not go to his wedding in his soiled work clothes, which is obvious to the point of pain and irritation. Occasionally the sentence structure is atrocious; nouns frequently appear as adjectives; and present participles are used when the English language has a perfectly good noun for the purpose.

The "cases" are readable but occupy far too much space for the points they make. Furthermore, they often represent fallacies of illustration. One can find a "case" to illustrate almost any point in human relations, and cases prove nothing about the frequency or typicality of a given situation.

Although much of the content is obvious, and although truisms are spun out so endlessly that they try one's patience, the chief merit of the book is its ballast, its moderation. Yet moderation and mediocrity need not be identical.

State Supervision of Local Government: Its development in Massachusetts. By Dale Pontius. With an introduction by Leverett Saltonstall. 8°, paper, 165 pp. Washington, D. C.: American Council on Public Affairs, 1942. $2.75 (paper), $3.25 (cloth).

This is a historical study of state administrative supervision of cities and towns in Massachusetts, covering a wide variety of activities, but devoting half its pages to education, health and welfare departments. In these particular fields it presents a faithful account of developments that are generally well known, documenting them in a very satisfactory way. An appreciative introduction by Governor Saltonstall adds to the interest with which a casual reader scans the pages. In the intricate field of political science this will constitute a very useful little volume. Medically, it has more interest for the layman than the physician, for the physicians of Massachusetts are generally well aware of the material it presents.

Clinical Roentgenology of Pregnancy. By William Snow, M.D. 4°, cloth, 178 pp., with 119 illustrations. Springfield, Illinois: Charles C Thomas, 1942. $4.50.

Radiology and obstetrics have been affiliated with each other for some time, but this book is the first to appear offering the combination to the medical profession in a single volume. The author emphasizes his desire to simplify procedures so that his teachings may be employed in the daily routine with obstetric patients.

The contents are divided into seven chapters, but the material is primarily divided into two main divisions: the study of the maternal pelvis and fetus, and the study of the soft structures of pregnancy. In the early chapters, the author briefly mentions the technics used by other men and then describes his own technic in great detail. The maternal pelvis is treated thoroughly, with his clinical observations included in each discussion. A slide rule has been devised using correction factors to correct for distortion of the image in the pelvimetric and cephalometric computations. Chapter five deals with the relation of the fetus to the pelvis. The author mentions the likely difficulties to consider at the inlet, midpelvis and outlet. The usual problems of the midpelvis are described in some detail, as well as the manner in which they relate to the anthropoid, android, platypelloid and gynecoid pelves.

Soft-tissue visualization, as related to pregnancy, is treated in the last chapter. The author claims to be able to recognize the site of the placenta, placenta previa, premature separation of the placenta, varying degrees of hydramnios, some tumors complicating pregnancy and extrauterine pregnancy by his methods. His technic frequently involves the injection of air into the bladder and rectum as an aid in outlining the soft-tissue structures.

Following the final chapter, there are twenty-two case reports in which his methods were employed. These are particularly useful in clarifying and in applying the material that has been presented in the previous chapters.

The book as a whole is certainly a useful contribution to the subject. However, there is reason to doubt that those who read it will find the application of the recommended methods quite so simple as the author intends. There are other technics, particularly in pelvimetry, that good authorities consider simpler, less time consuming and possibly more accurate. Furthermore, the author's technic of taking the lateral film with the patient lying on her side is open to considerable variance of opinion. Most people today agree that a lateral film taken in the upright position is far more accurate and useful from an obstetric viewpoint, although its use in active labor has been completely overlooked.

Textbook of Clinical Parasitology, including Laboratory Identification and Technic. By David L. Belding, M.D. 4°, cloth, 888 pp., with 1356 illustrations and 4 color plates. New York: D. Appleton-Century Company, Incorporated, 1942. $8.50.

This textbook is comprehensive and has been prepared with meticulous care. The text not only describes the parasites but also includes much information on diagnosis, prevention and treatment. The style is clear and succinct, and the many illustrations are notable for their excellence.

The text is supplemented by numerous charts, diagrams and tables. These must have added considerably to the cost of the volume, and the reviewer believes that some of this material might well have been omitted.

The subject of human parasitology is well presented, and the book should prove very valuable to students, practitioners and specialists.

Preventive Medicine in Modern Practice. Edited under the auspices of the Committee on Public Health Relations of the New York Academy of Medicine. By James A. Miller, Sc.D., M.D., D.P.H.; George Baehr, M.D.; and E. H. L. Corwin, Ph.D. Third edition. 4°, cloth, 851 pp., with 22 illustrations and 37 tables. New York: Paul B. Hoeber, Incorporated, 1942. $10.00.

This is not a textbook of preventive medicine, but "an attempt to combine in one volume the clinical and environmental aspects of health problems in a manner suited to the needs of both the general practitioner and the specialist." The defect most obvious in such a synthesis is well expressed by one of the fifty distinguished coauthors, Dr. Edgar van Nuys Allen, who contributes the chapter on degenerative diseases, "In the light of present knowledge there is too little fact and too much fancy, too little evidence and too much opinion, and too little knowledge and too many questions."

The book is divided into four sections: sociobiological aspects, clinical aspects, environmental aspects and organizational aspects. It is inevitable that there should be considerable variation in the quality of the many chapters. Of outstanding interest and value are the following: "The Prevalence of Disease," by Haven Emerson; "Tuberculosis," by James A. Miller; "Heart Disease," by Paul D. White and "Provision for the Care of the Sick," by Ray Lyman Wilbur.

It can be heartily recommended to the practitioner of medicine as a means of orienting himself in a field that is certain to be invaded in progressively larger numbers by an army of zealots who will seek to dominate it by legislative and political measures. It is not recommended as a satisfactory text for medical students.

History of the School of Nursing of the Presbyterian Hospital, New York: 1892–1942. By Eleanor Lee, A.B., R.N. 8°, cloth, 286 pp., with 58 illustrations. New York: G. P. Putnam's Sons, 1942. $3.50.

This is an excellent history of the development of the nursing school in one of the leading hospitals in the country. Of particular value are the illustrations. Miss Lee seems to have found many of them, and not a few may be considered unique. There is, for instance, an excellent picture of the operating theater in 1903, and another showing the parade of the American nurses in Paris on July 4, 1918. This is a book, therefore, that will have an appeal far beyond the average history of a hospital nursing corps. It is a historical document of considerable importance and should find its way into all medical libraries, as well as into the hands of physicians interested in medical history.

Standard Radiographic Positions. By Nancy Davies, M.S.R., and Ursel Isenburg, M.S.R. 8°, cloth, 136 pp., with 103 illustrations. Baltimore: The Williams and Wilkins Company, 1942. $2.00.

This small book deals with the positioning of patients for roentgen examination and was written by two English technicians. It is stated in the preface that there was real need for such a book in England. Whether or not that be true, there seems to be little need for publishing it in this country since it adds nothing to the standard American texts on x-ray technic.

There is a simple statement concerning how the patient should be placed for each examination, and there is a sketch depicting the end result; but there are no photographs to show clearly the patient in the desired position, and no attempt has been made to reproduce the resulting radiograph.

Health Education of the Public: A practical manual of technic. By W. W. Bauer, M.D., and Thomas G. Hull, Ph.D. Second edition, revised. 8°, cloth, 315 pp., with 52 illustrations. Philadelphia: W. B. Saunders Company, 1942. $2.75.

This volume has been compiled in an effort to help physicians who are preparing medical material for the use of the public. It covers chapters on the radio, the exhibit, the meeting, the pamphlet, the newspaper, the magazine article, the motion picture and the use of stereopticon slides. Detailed information on all phases of health information is given, such as, samples of the different sizes of type, criticism of posters, the making of stereopticon slides, the cost of printing pamphlets and the arranging for public meetings.

Of particular interest are the pages devoted to technical words used in articles written for the public. These words are divided into four groups — those which should not be used and for which a synonym is available, those which must be used because of a lack of a proper synonym, those which are technical but also familiar and can be used, and those which under no circumstances should be used.

In the foreword of the book Morris Fishbein states, "The physician or the worker in the field of public health will find here opportunity to accumulate in a short time knowledge which otherwise might be gained only with great difficulty and at considerable expense by the old system of trial and error."

This book can be recommended to all physicians helping to educate the public on medical subjects and to nonmedical workers in health education.

Urology in War: Wounds and other emergencies of the genito-urinary organs, surgical and medical. By Lieutenant Commander Charles Y. Bidgood (MC), U.S.N.R. 8°, cloth, 78 pp., with 27 illustrations and 3 tables. Baltimore: The Williams and Wilkins Company, 1942. $2.00.

This book describes, in condensed form, the essential features of traumatic lesions and inflammatory conditions of the genitourinary tract, and acute nontraumatic and noninflammatory lesions of the penis and scrotal contents. Brief review of the regional anatomy is included, and the treatment of each condition is outlined. There is a chapter on acute retention, one by Lloyd Lewis on bladder dysfunction after cerebrospinal injury, and one by Ralph Tovell on anesthesia in urology.

Although the material is condensed, it is sufficiently explicit to enable any intelligent medical officer to apply the principles in actual practice. The illustrations by Didusch are, of course, excellent and help greatly in clarifying the operative technic.

A few criticisms are worth noting. For example, the use of sulfathiazole in the peritoneal cavity (page 13) is not generally approved, sulfanilamide being preferred. In a perineal operation for stricture, the reviewer believes that simple longitudinal incision of the floor of the urethra through the stricture is more practical than an attempt to dissect the scar tissue off the outer wall of the urethra (page 40), since a stricture involves the mucosa, and the close approximation of the vascular tissue of the corpus spongiosum is likely to make such an attempt result in profuse hemorrhage. Aside from these minor criticisms, the book is consistent with the generally accepted views of urologists; it should prove helpful in emergencies involving the genitourinary tract.

(Notices on page x)